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Linkage

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IN THIS ISSUE:

New Technique May Markedly Improve Measurement of Endogenous Estrogens and Metabolites, **4**

DCEG Investigators Gather Awards at NCI Ceremony, **6**

Core Genotyping Facility Launches Laboratory Information Management System, **7**

HHMI – NIH Scholars Gain Epidemiology Research Experience, **8**

Award Lectures at the Annual NCI Intramural Retreat, **10**

SEER Cancer Registry Celebrates 30 Years, **11**

Scientific Highlights, **12**

DCEG People in the News, **18**

Comings … Goings, **21**

Epidemiology Featured at NIH Research Festival, **24**

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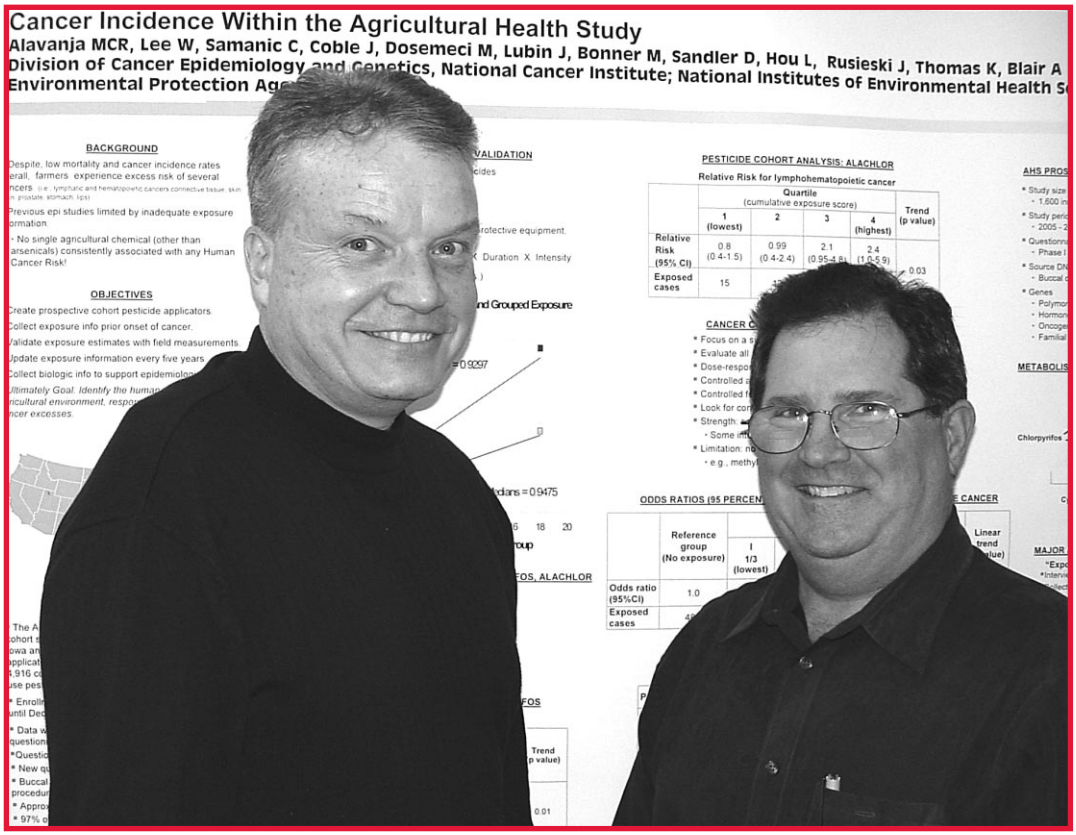
Agricultural Health Study Aims To Clarify Cancer–Pesticide Association

Despite better overall health than the general population, several studies have shown that farmers and other agricultural workers face an increased risk for certain cancers, including lymphoproliferative malignancies and cancers of the skin, lip, stomach, brain, connective tissue, and prostate. Farmers also appear more likely to suffer from certain respiratory ailments and some renal and neurological diseases.

Past studies of farm workers were either case-control design studies, for which concern exists about case-response bias regarding exposure, or retrospective cohort design studies, for which few details regarding agricultural exposure or other disease risk factors were typically available. Against this backdrop, the Occupational and Environmental Epidemiology Branch (OEEB) developed the Agricultural Health Study (AHS) in 1993. **Michael Alavanja, Dr.P.H.**, is principal investigator for the study, which is being carried out through collaborative efforts at the University of Iowa, led by Dr. Charles Lynch, and the Battelle Centers for Public Health Research and Evaluation in North Carolina, led by Mr. Charles Knott. The study is a cross-agency effort being conducted in partnership with the National Institute of Environmental Health



Michael Alavanja and Aaron Blair

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Sciences, led by Dr. Dale Sandler, the Environmental Protection Agency, led by Mr. Kent Thomas, and the National Institute for Occupational Safety and Health, led by Ms. Cynthia Hines.

The AHS is a large-scale prospective cohort study of nearly 60,000 private and commercial pesticide applicators and 30,000 of their spouses that is designed to evaluate the effects of environmental, occupational, genetic, and dietary factors on the health of farmers and their families in Iowa and North Carolina. Researchers hope the study will shed light on cancer etiology and provide information that agricultural workers can use to make informed health decisions.

AHS Aims

A variety of environmental factors may contribute to the increased incidence among farmers and other agricultural workers of certain cancers and other diseases. These include prolonged exposure to sunlight, dust, solvents, engine exhaust, fuels, oils, animal viruses, mycotoxins, contaminated drinking water, and pesticides. Of these many exposures, the potential link between pesticides and cancer has received the most attention to date, but there is also concern about other exposures and diseases.

"The Agricultural Health Study is the capstone of a major area of research for DCEG," said **Aaron Blair, Ph.D.**, Chief of OEEB and author of many scientific publications on the health effects of pesticides. "The prospective design, with detailed information on agricultural exposures and rural lifestyle factors and with biologic specimens to assess gene-exposure interactions, will allow evaluation of potentially hazardous chemicals that may impact the health of the general population as well as farm families."

Researchers chose Iowa and North Carolina as study locations due to their strong agricultural sectors, diverse production methods, commodities, and products.

The AHS began in 1993 with recruitment of the study cohort and collection of questionnaires with detailed information about farming, including types of crops grown, livestock raised, pesticide use, medical conditions, and lifestyle factors. The AHS team is now validating questionnaire-based exposure assessment with comprehensive field measurements of pesticides and continuing follow up for mortality and cancer incidence, collecting additional information by interview, and collecting buccal cells as a source of germline DNA.

From now through 2008, the AHS will accrue more than 1 million person-years of follow up, and 5,000 incident cancer cases will be available for analysis. With the survey scheduled to continue through 2013, participants will be contacted to update information on exposures, collect data on selected disease outcomes, and continue follow up for mortality and cancer incidence. Researchers will focus on risk factors and mechanisms of disease action by

Photo by Scott Bauer (Agricultural Research Services/USDA)

"The AHS has already yielded results on cancer and other outcomes. The first major cancer finding, published in the May 1, 2003, issue of the *American Journal of Epidemiology*, showed a 14 percent greater risk of developing prostate cancer among more than 55,000 male pesticide applicators."

integrating nested case-control studies with a variety of biological markers.

New Findings

The AHS has already yielded results on cancer and other outcomes. The first major cancer finding, published in the May 1, 2003, issue of the *American Journal of Epidemiology*, showed a 14 percent greater risk of developing prostate cancer among more than 55,000 male pesticide applicators. Elevated risks were seen for methyl bromide, which is used to fumigate soil and stored grains, and for chlorinated pesticides. The analysis also linked exposure to five other chemicals to an increased risk of prostate cancer among men with positive family histories. "Farming is the most consistent occupational risk factor for prostate cancer," Dr. Alavanja noted. "And this finding suggests that, for some men, a genetic predisposition to prostate cancer makes them especially susceptible when exposed to certain pesticides."

In a recent study of other disease end-points, associations have been uncovered between fungicides and increased risk of macular degeneration, and several pesticides and respiratory wheeze.

Next Steps

Analyses are now under way to evaluate the potential link between various classes of pesticides and cancers of the lung, breast, colon, ovary, and lymphatic tissues. As for the future, Dr. Alavanja said, "the AHS will help clarify if there is an association between pesticide exposure and cancer risk, an issue that has remained elusive since the 1940s. In the next 5 years, I foresee AHS generating definitive data on this issue as well as other exposures prevalent in the agricultural environment."

For more information on the AHS, please visit *http://www.aghealth.org/* ■

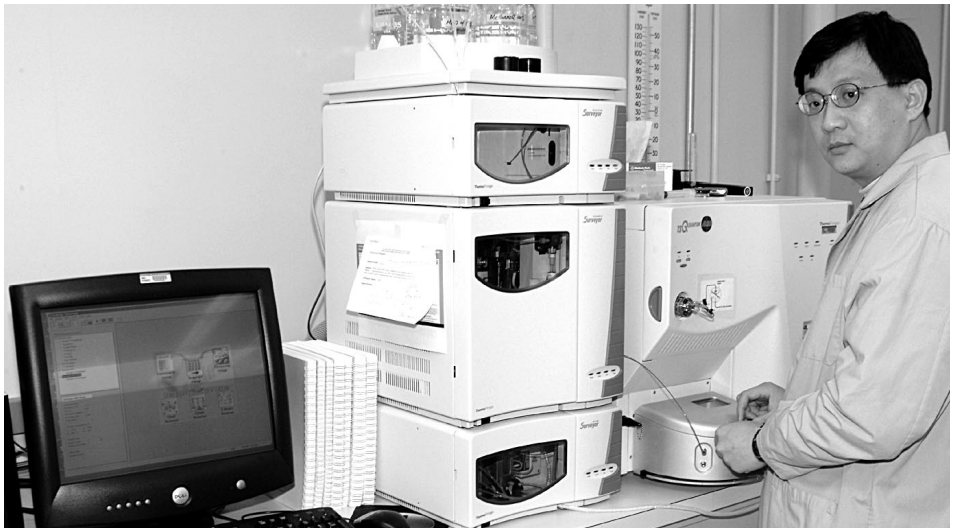
—Jill Giannessi

NEW TECHNIQUE MAY MARKEDLY IMPROVE MEASUREMENT OF ENDOGENOUS ESTROGENS AND METABOLITES

DCEG researchers are playing key roles in developing a new assay that promises to greatly improve the accuracy, speed, and cost of measuring endogenous hormones in biologic samples. The method pairs high performance liquid chromatography (HPLC) with mass spectrometry (MS), a combination, called LC-MS, that has not been used to measure steroid hormones.

"For decades, researchers in hormonal carcinogenesis have been aware that more accurate and efficient methods of measuring endogenous levels of hormones and hormone metabolites were needed to advance the field," said **Robert Hoover, M.D., Dr.P.H.**, Director of the Epidemiology and Biostatistics Program in DCEG. "This method is likely to be a leap forward, not only for cancer research but also for myriad medical conditions related to steroid hormones. In addition, quantifying estrogen exposure and metabolism by this method may identify women at high risk of breast cancer more accurately than the questionnaire-based risk factors currently used."

Commercial kits now used to measure endogenous estrogens rely on immunoassays and have poor specificity due to antibody cross-reactivity and large variability due to changing lots and sources. With these kits, each estrogen or estrogen metabolite is measured separately; each analyte costs around $100 and requires between 0.2 ml and 1.0 ml of sample. In contrast, gas chromatography-mass spectrometry (GC-MS), which has been considered the gold standard, is a direct and more accurate method for measuring hormones. GC-MS requires extensive, laborious, time-consuming sample preparation, however, and is not only expensive—on the order of $1000 per single analysis—but can require 10 ml or more of sample from each subject. A year would be required to assay 500 samples. Such constraints limit the application of these techniques to epidemiology studies.



Xia Xu performs an assay on the TSQ-Quantum LC-MS analyzer

"Cancers of the breast, ovary, endometrium, and prostate are all likely to be related to endogenous levels of steroid hormones, while other sites, such as colon, gallbladder, testis, and thyroid, may be associated as well," said **Regina Ziegler, Ph.D., M.P.H.**, senior investigator in DCEG. "An accurate and efficient way to measure circulating and tissue-specific hormone levels could advance our understanding of the etiology of these cancers and lead to improvements in prevention and treatment."

The challenge of developing a highly sensitive, accurate, reliable, and rapid method for measuring endogenous estrogens and their metabolites in biological samples intrigued **Xia Xu, B.M., Ph.D.**, who joined the Hormonal and Reproductive Epidemiology Branch (HREB) in 2000 as a postdoctoral fellow. Dr. Xu, who holds degrees in medicine and toxicology, had previously measured estrogens and phytoestrogens using GC-MS. "LC-MS is an amazingly powerful tool for separating, identifying, and measuring compounds with very similar structures," noted Dr. Xu. "However, MS only detects ionized—or charged—molecules, and estrogens, which are fat-soluble, are not charged."

Larry Keefer, Ph.D., an organic chemist and Chief of the Laboratory of Comparative Carcinogenesis at the NCI Center for Cancer Research, offered Dr. Xu laboratory space and supplies so he could start his LC-MS experiments. Drs. Xu, Keefer, and Ziegler realized they faced two hurdles: first, finding a chemical derivatization that would add charge to the neutral estrogens, and second, identifying a way to completely separate individual estrogen metabolites, many of which share the same molecular weight and similar MS fragmentation patterns. To further complicate the situation, the techniques needed to work in complex biological matrices, with limited quantities of material, and in a manner that was robust and simple enough to be automated.

To solve the first problem, the team evaluated various chemical techniques for quantitatively adding bulky charged moieties to each estrogen metabolite. Eventually, they found something that worked—adding a hydrazone at the C-17 carbonyl group of catechol estrogens.

This approach is so novel that the NCI Technology Transfer Branch decided to apply for patent coverage for this work. Another derivatization is being developed to facilitate analysis of hormones that do not have C-17 carbonyl groups. The second problem was solved by pairing LC with MS because LC requires very little sample, can separate charged molecules, and takes advantage of rapidly emerging technology.

The LC-MS combination has proven so successful that all 16 common estrogens and estrogen metabolites in urine can be measured in 30 minutes with less than half a milliliter of sample. Because of the technique's sensitivity, Dr. Xu has been able to isolate and describe a urinary estrogen metabolite not previously reported in non-pregnant women. The research team published details of their technique in the November 2002 issue of the *Journal of Chromatography B;* a second paper with more details is being submitted for publication.

The researchers initially focused on urine samples, which contain fewer interfering substances than serum or plasma. They anticipate, however, that the technique will be applicable to plasma, serum, and possibly tissue. A modified approach should work with androgens, phytoestrogens, and estrogens. Similar LC-MS methodology may also apply to separating, identifying, and measuring structurally similar peptide hormones such as prolactins and insulin-like growth factors.

"This technique could be immediately applicable to a number of DCEG studies that are measuring endogenous hormone levels," said **Louise Brinton, Ph.D.**, Chief of HREB. Although enthusiasm among the investigators is high, work is still needed to determine the method's ultimate utility. In addition to extending the method to blood and tissue samples, robotic procedures must be developed to enable high throughput. Validity, reliability, and sensitivity must be demonstrated with large numbers of field samples, and the ultimate cost per sample needs to be determined. To expedite this research, Dr. Xu has moved to the new Laboratory of Proteomics and Analytical Technologies (LPAT) at NCI-Frederick, where he will be able to use powerful mass spectrometry equipment and the expertise of scientists specialized in this field. The DCEG hormone measurement project has become an important part of small molecule mass spectrometry research in LPAT.

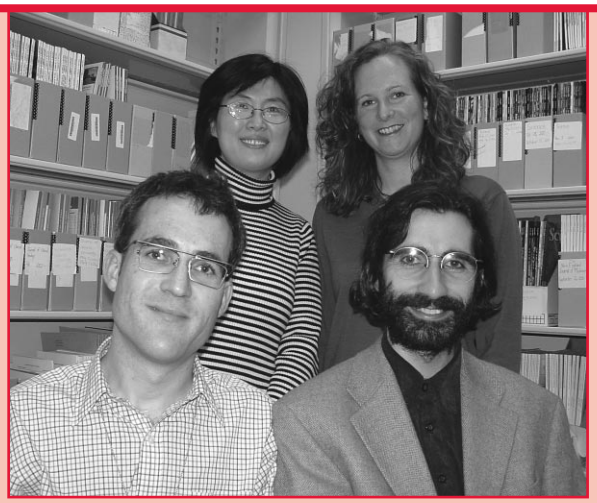
Larry Keefer, Xia Xu, Timothy Veenstra, Regina Ziegler

"While proteomics dominates the research conducted within the LPAT at present, we fully understand the need for measuring small molecules since metabolites as well as proteins play a critical role in cancer etiology," says Timothy Veenstra, Ph.D., the LPAT Director. "Continuing developments in the field of mass spectrometry will enable us to measure small molecules directly, quantitatively, and rapidly at levels of sensitivity previously not possible." ■

—Maria Sgambati, M.D.

DCEG FELLOWS TAKE HOME NIH RESEARCH AWARDS

In October, four DCEG scientists received NIH Fellows Awards for Research Excellence (FARE). The awards recognize outstanding scientific research by fellows in the NIH intramural research program. To enter, fellows must submit abstracts of their research, which are peer reviewed by a blinded study section. Competition was stiff this year, with more than 1,000 fellows applying for the award and less than 25 percent of applicants receiving an award.



FARE Winners: Michael Hauptmann, Juan Alguacil; Lifang Hou, Beth Brown

In the Occupational and Environmental Epidemiology Branch, **Juan Alguacil, M.D.**, won for his work relating urinary pH and cigarette smoking to bladder cancer risk, and **Lifang Hou, M.D., Ph.D.**, for her project on the risk of colorectal adenomas in relation to smoking and *CYP1A1* and *NQO1* polymorphisms. **Elizabeth Brown, Ph.D., M.P.H.**, of the Viral Epidemiology Branch, was recognized for her study evaluating determinants of human herpesvirus-8 viremia in the general population, and **Michael Hauptmann, Ph.D.**, of the Biostatistics Branch, for his work examining mortality from lymphoproliferative malignancies among workers in the formaldehyde industry.

Begun in 1995, the FARE competition is sponsored by the NIH Fellows Committee, the NIH Scientific Directors, the NIH Office of Research on Women's Health, and the NIH Office of Education. Winners receive a travel stipend to attend a scientific meeting, at which they present their papers in a symposium or poster session.

DCEG INVESTIGATORS GATHER AWARDS AT NCI CEREMONY

DCEG staff members won several individual and group awards at the annual NCI ceremony held October 9th. **Robert Hoover, M.D., Sc.D.**, received the NCI Director's Gold Star, a new award this year that recognizes a special accomplishment that advances the NCI agenda in a significant or meaningful way. Dr. Hoover was acknowledged for his leadership in adhering to a scientific focus during the NCI Workshop on Early Reproductive Events and Breast Cancer.

NIH Merit Awards went to eight DCEG researchers. In the Biostatistics Branch, **Nilanjan Chatterjee, Ph.D.**, won for his work in developing new designs and analysis methods for epidemiologic research, and **Ruth Pfeiffer, Ph.D.**, was recognized for her innovative statistical methods that enhance the usefulness of genetic and molecular data in epidemiologic research. **Ethel Gilbert, Ph.D.**, of the Radiation Epidemiology Branch, was recognized for her landmark research on second cancers, thyroid cancer risks associated with I-131 fallout, and cancer risks among nuclear and electrical utility workers, and **Gladys Glenn, M.D., Ph.D.**, of the Genetic Epidemiology Branch (GEB), won for her clinical expertise in the investigation and care of high-risk families with renal cancers. **Andrew Bergen, Ph.D.**, was recognized for developing the design specifications and overseeing the implementation of a laboratory information management system for the NCI Core Genotyping Facility. **Jorge Toro, M.D.**, of the GEB, won a Public Health Service Commendation Medal for his work on hereditary leiomyomatosis and renal cell cancer (HLRCC) and the Birt-Hogg-Dubé syndrome.

Three members of the Clinical Genetics Branch won a Group Award: **Jennifer**

Robert Hoover receives special medal from Andrew von Eschenbach

NCI Merit Awards: Ethel Gilbert, June Peters, Ruth Pfeiffer, Nilanjan Chatterjee, Jorge Toro, Jennifer Loud, Nancy Weissman, Gladys Glenn

NCI Group Merit Award: Elyse Wiszneauckas, Marianne Henderson, Chitra Mohla

Loud, M.S.N., C.R.N.P., for extraordinary contributions to creating the clinical research component of the Branch's familial cancer research program; **June Peters, M.S.**, for authoritative comprehensive clinical cancer genetic counseling and education materials; and **Nancy Weissman, M.S.S.W.**, for creative leadership in establishing the Branch's portfolio of behavioral and psychosocial research studies targeting people at increased genetic risk of cancer. An NIH Group Award also went to **Marianne Henderson, M.S.**, **Chitra Mohla, M.S.**, and **Elyse Wiszneauckas** of the DCEG Office of Division Operations and Analysis for exceptional initiative in developing a Web-based application to help manage and support intramural research studies. In addition, **Louise Brinton, Ph.D.**, Chief of the Hormonal and Reproductive Epidemiology Branch, and Dr. Hoover also received a Group Award, along with staff from other parts of the NCI, for their work in planning and implementing the NCI Workshop on Early Reproductive Events and Breast Cancer. ■

CORE GENOTYPING FACILITY LAUNCHES LABORATORY INFORMATION MANAGEMENT SYSTEM

The NCI Core Genotyping Facility (CGF), whose mission is to meet the high-throughput genotyping and DNA sequencing needs of DCEG and NCI's Center for Cancer Research, launched a new Laboratory Information Management System (LIMS) last fall. The project is the culmination of 2 years of work that has taken the LIMS from design to debugging.

The focus of LIMS development has been to construct a single relational database application that could track all laboratory processes, store genomic and related laboratory data, and provide web-based access to data at every step of each CGF laboratory process. Data include information on DNA samples (location, quantification, sequencing, and genotyping), molecular assay reagents, and sequence annotations from CGF and the National Center for Biotechnology Information. The LIMS laboratory process support will replace a laboratory data management system that relied on unintegrated programming and databases.

"The focus of LIMS development has been to construct a single relational database application that could track all laboratory processes, store genomic and related laboratory data, and provide web-based access to data at every step of each CGF laboratory process."

The CGF LIMS will help staff work more efficiently in *in silico* (dry) and molecular genetic (wet) laboratory processes, and provide opportunities to add quality control measures through the systematic analysis of laboratory procedures. Because it is a single database application, the LIMS will integrate and greatly simplify the receipt, import, administration, review, analysis, and reporting of millions of laboratory samples and associated data points.

Development of this critical tool has been a collaborative project involving CGF bioinformaticists, geneticists, and technical staff working with programmers from LabVantage, Inc., of Bridgewater, NJ, the private-sector contractor selected to help create LIMS. Implementation has consisted of collaborative data-model design, functional requirements, software configuration and installation, and debugging. CGF personnel are learning to use the new system by moving data from the old laboratory data management system to the LIMS; this also allows them to test the software, update the data model, and reconfigure the software to match laboratory process changes and improve LIMS function and user interaction.

The following CGF staff should be congratulated on this achievement: **Michael Beerman**, **Andrew Bergen, Ph.D.**, **Stephen Chanock, M.D.** (CGF Director), **Andrew Crenshaw**, **Cynthia Glaser, M.S.**, **Amy Hutchinson**, **Edward Miller, M.S.**, **Bernice Packer**, **Liqun Qi**, **Hughes Sicotte, Ph.D.**, **Brian Staats**, **Robert Welch, M.S.** (Deputy Director), **Sunita Yadavalli, M.S.**, and **Meredith Yeager, Ph.D.** (Managing Director).

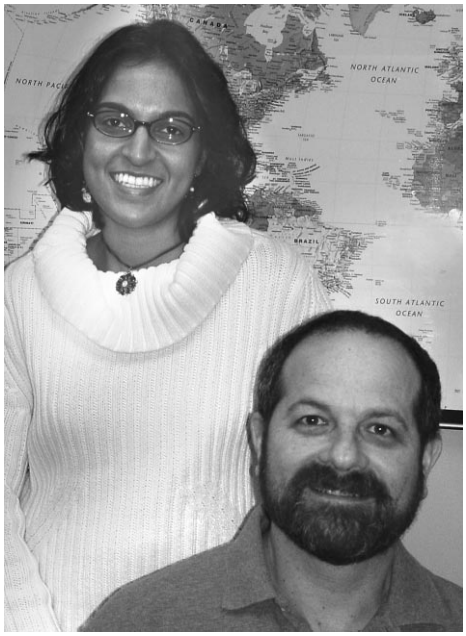
—Andrew Bergen

HHMI – NIH SCHOLARS GAIN EPIDEMIOLOGY RESEARCH EXPERIENCE

DCEG is hosting two medical students who are part of the prestigious Howard Hughes Medical Institute (HHMI)-NIH Research Scholars Program. **Randi Cohen**, from the State University of New York at Stony Brook, is working in the Radiation Epidemiology Branch (REB); **Michelle Khan**, from the University of Medicine and Dentistry of New Jersey (UMDNJ), is in the Hormonal and Reproductive Epidemiology Branch (HREB).

Ms. Khan's experience with HHMI dates back to her undergraduate years at Duke University, when she spent a summer in the Howard Hughes Research Fellows Program working in biochemistry and structural molecular biology. After graduating *cum laude* with a double major in chemistry and Spanish, she began an M.D./M.P.H. program at UMDNJ. Her interest in epidemiology developed during the summer between her first and second year of medical school when she did clinical research on uterine fibroids with Dr. Gloria Bachmann at the Women's Health Institute, Robert Wood Johnson Medical School. "I enjoyed my time doing research that summer," said Ms. Khan. "I wanted to explore epidemiologic research in more depth as a potential career path, which is why I chose to apply to the HHMI-NIH Research Scholars Program."

Ms. Khan is spending her year at DCEG investigating human papillomavirus (HPV) natural history and diagnostics with **Mark Schiffman, M.D., M.P.H.** Approximately 5–20 HPV subtypes cause cervical cancer, and Ms. Khan is trying to clarify the role of HPV types with low etiologic fractions using data from DCEG cohort studies. By analyzing which combination of types should be assayed, she hopes to understand how to maximize the tradeoff between screening sensitivity and specificity.



HHMI scholar Michelle Khan with mentor Mark Schiffman

When asked about Ms. Khan, Dr. Schiffman responded enthusiastically. "Michelle is so smart that it's a pleasure to introduce her to topics I love," he said. "She likes statistical thinking, which will color the rest of her medical training. I hope she returns here someday."

Ms. Khan agrees that the year has been a wonderful experience so far. "I have learned a great deal in the 4 months since starting at DCEG. The mentoring here is unparalleled in my experience… the HPV group is very enthusiastic about letting junior researchers take part in projects and generous when it comes to teaching."

Ms. Khan has also taken the opportunity to explore issues in clinical epidemiology and genetics. Through the mentorship of **Mark H. Greene, M.D.**, in the Clinical Genetics Branch, she shadows staff members, including **Jennifer Loud, M.S.N., C.R.N.P.**, **Gladys Glenn, M.D., Ph.D.**, and **June Peters, M.S., C.G.C.**, during visits to their clinics.

Ms. Cohen, the second HHMI scholar, attended the Massachusetts Institute of Technology (MIT), receiving bachelor's (2000) and master's (2001) degrees in nuclear engineering. The research topic for her undergraduate thesis was "Shielding Reduction Factors for the MIT Nuclear Reactor Lab," and she became licensed as a senior reactor operator. For her master's degree, Ms. Cohen worked on a joint project involving the nuclear and environmental engineering departments to study bacterial reduction of uranium and plutonium. During this period, she realized that she was more interested in the medical uses of radiation and decided to pursue an M.D. degree.

During her first 2 years of medical school, Ms. Cohen developed an interest in biomedical research, which prompted her to apply to the HHMI-NIH program. After being accepted, she began searching for a group that worked on challenging projects and offered a supportive research environment with good mentorship. Hoping to combine nuclear engineering and medicine, she selected REB because the "branch goals were very similar to my own interests. The REB also provided a variety of interesting projects, dedication to teaching and mentorship, and enthusiasm for their work."

Ms. Cohen is working on several cancer survivorship projects that focus on second primary cancers. Under the mentorship of **Lois Travis, M.D., Sc.D.**, Ms. Cohen is conducting a long-term follow-up study of more than 40,000 men with testicular cancer from several international cancer registries, and analytic studies of second cancers following malignancies of the stomach and pancreas. These investigations will provide important new information about the role of radiation and chemotherapy dose, especially cisplatin, and their interactions in the development of

HHMI scholar Randi Cohen with mentor Lois Travis

secondary cancers. Ms. Cohen is also working with **Rochelle Curtis, M.A.**, **Peter Inskip, Sc.D.**, and **Joseph Fraumeni, M.D.**, to quantify the risk of second cancers in childhood cancer patients treated for soft tissue sarcoma, and is helping write a chapter on this topic for the Surveillance, Epidemiology, and End Results Multiple Primary Cancer Monograph.

"My experience so far has been amazing," said Ms. Cohen. "I greatly enjoy working in DCEG and especially working with wonderful, dedicated individuals who are happy to offer their experience and mentorship." Her NCI mentors welcome her enthusiastic approach, comprehensive background in radiation, and ability to quickly comprehend epidemiologic issues. "Randi's input into epidemiologic studies to date has been extraordinarily helpful and highly valued," noted Dr. Travis. "Given her unique talents, we hope that she decides to pursue a career in cancer epidemiology."

The HHMI-NIH Research Scholars Program was established in 1985 to give outstanding students at U.S. medical and dental schools the opportunity to receive research training at NIH. Research scholars spend 9 months to a year at NIH, conducting basic, translational, or applied biomedical research under the mentorship of senior NIH research scientists. This year, the program received 179 applications and accepted 42 students. Students can choose from 1,200 tenured or tenure-track intramural scientists working on more than 2,500 research projects in six primary areas of interest: neuroscience, cell biology, structural biology, immunology, epidemiology/biostatistics, and genetics.

"Although the basic science areas tend to be quite popular, I think a growing number of medical students are becoming interested in the field of epidemiology and public health," noted Ms. Khan.

For more information on the HHMI-NIH program, please visit *http://www.hhmi.org/*. ■

—Rochelle Curtis, Mark Schiffman, and Lois Travis

RADIATION EPIDEMIOLOGY SHORT COURSE AND LECTURE SERIES

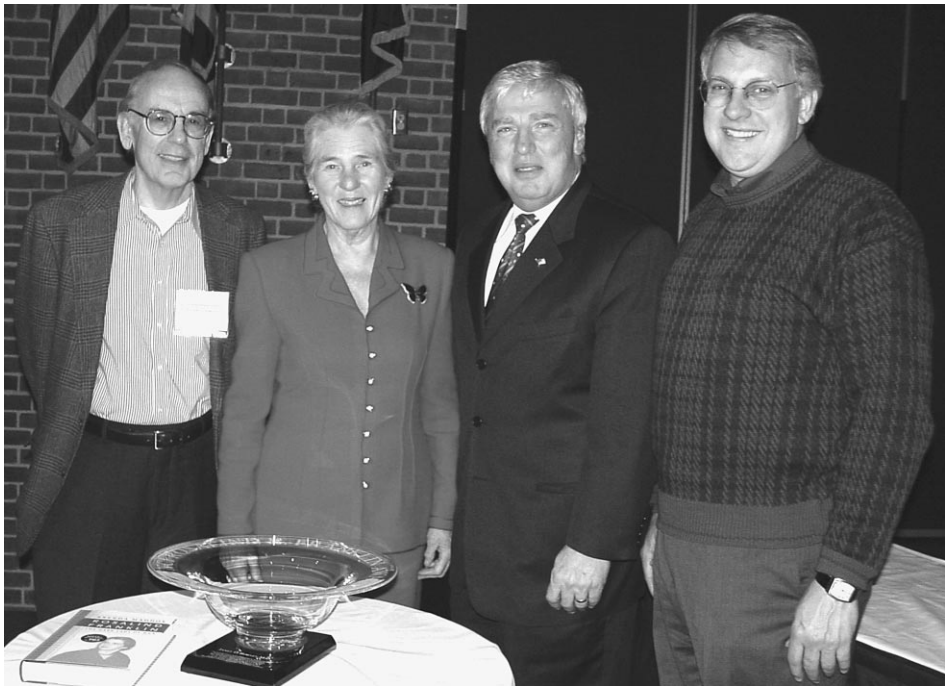
Under the direction of Peter Inskip, Sc.D., the Radiation Epidemiology Branch will offer a short course from May 4 to 14 on a variety of topics in radiation epidemiology. Speakers include NCI staff and scientists from other government agencies and academic institutions. The course is intended for those who have epidemiology backgrounds and are interested in the health effects of exposure to radiation, particularly the relationship between ionizing radiation and cancer. The course is free but advance registration is required.

The program offers an overview of the radiation epidemiology field with a focus on radiation-related cancer. It begins with basic radiation physics, dosimetry, radiation chemistry, and radiobiology, and continues with presentations on epidemiologic studies of radiation-exposed populations, including atomic bomb survivors in Japan, medically irradiated populations, and persons with occupational or environmental radiation exposures. Methods for quantifying radiation risks, the use of such information in setting radiation protection standards, and risk communication also will be discussed. The course focuses on ionizing radiation but also considers nonionizing radiation. Throughout the course, instructors will stress the importance of radiation dosimetry in epidemiologic studies and highlight key methodologic issues, including challenges in the study of low-dose effects. Possible new sources of radiation exposure and their potential risks will be covered.

For more information on the Radiation Epidemiology Course, please visit: *http://dceg.cancer.gov/epicourse.html.*

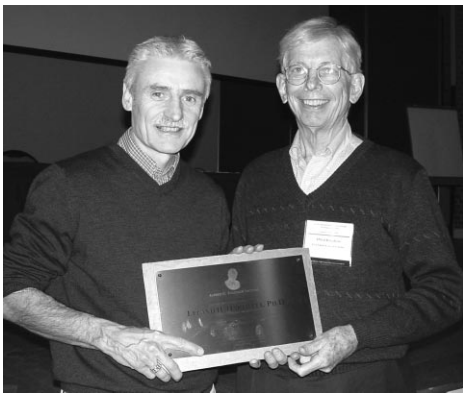
AWARD LECTURES AT THE ANNUAL NCI INTRAMURAL RETREAT

Janet D. Rowley, M.D., delivered the Rosalind E. Franklin Award Lecture for Women in Cancer Research, which was given at the annual NCI Combined Retreat in January. Dr. Rowley is renowned for seminal discoveries at the University of Chicago, linking chromosomal translocations to the development of leukemia. The NCI prize honors the commitment of women in cancer research and is given in tribute to Dr. Franklin, who played a central role in the discovery of the DNA double helix. Dr. Rowley was introduced by **Martha Linet, M.D., M.P.H**, Chief of the Radiation Epidemiology Branch.



Rosalind Franklin Award: Joseph F. Fraumeni, Jr., Janet Rowley, Andrew von Eschenbach, J. Carl Barrett

The second honorary lecture at the retreat was the Alfred G. Knudson Award Lecture in Cancer Genetics. This prize is given in tribute to Dr. Knudson, who developed mathematical models that revolutionized the understanding of the genetic basis of cancer. Dr. Knudson served at NCI in the late 1990s and continues to participate each year in the retreat. This year's recipient was Nobel Laureate Leland H. Hartwell, Ph.D., President of the Fred Hutchinson Cancer Research Center in Seattle. He was honored for pioneering genetic and molecular studies uncovering the regulation of cell division. NCI Director Dr. Andrew von Eschenbach introduced Dr. Hartwell. ■



Knudson Award: Leland Hartwell and Alfred Knudson

MENTORING FOCUS OF ANNUAL ETHICS TRAINING

The fourth annual NIH training workshops on the responsible conduct of research focused on mentoring issues. The training, which is based on case studies, is required by all NIH employees involved in research and has previously covered issues related to scientific misconduct and authorship. This year's case study prompted thoughtful discussions about the impact of different mentoring styles, the need for mentoring throughout one's career, and the importance of training in good mentoring skills.

Ten DCEG staff members served as facilitators for the sessions. Recognition and appreciation for volunteering their time and skills to facilitate the discussions go to: **Chitra Mohla, M.S., Melinda Butsch-Kovacic, Ph.D., Joseph Coble, Sc.D., Joanne Colt, M.P.H., M.S., Dalsu Baris, M.D., Ph.D., Michie Hisada, M.D., Ph.D., Sc.D., Allan Hildesheim, Ph.D., Ursula Leitzmann, M.A.,** and **Sheree Hawkins**.

Resources related to mentoring are available in the library (located in Suite 350 in EPS) and on the following Web sites:

NIH Guide to Training and Mentoring
http://www1.od.nih.gov/oir/sourcebook/ethic-conduct/mentor-guide.htm

National Academy of Sciences: Advisor, Teacher, Role Model and Friend
http://www.nap.edu/readingroom/books/mentor/index.html

Science Magazine: Next Wave – Search on 'mentoring'
http://nextwave.sciencemag.org/

Linkage: Mentoring on the Move (December 1998)
http://dceg2.cancer.gov/newsletter/News1298.html

—Kristin Kiser, M.H.A

SEER CANCER REGISTRY CELEBRATES 30 YEARS

Last October, cancer researchers and administrators from around the country gathered at the NIH campus to mark the 30th anniversary of the Surveillance, Epidemiology, and End Results Program, better known as the SEER Program. The day of celebration included a mini-symposium with a seminar on health services and outcome research, and brief addresses from leaders in the cancer surveillance field. Cancer pattern surveillance is the foundation of the SEER network. It has been the primary means of measuring the national burden of cancer through incidence, survival statistics, and evaluation of the impact of cancer risk factors.

The celebration emphasized the program's scientific contributions to cancer control and public health in the United States and internationally, and honored those who have made such advances possible. In addition, the SEER registries were recognized for their remarkable commitment to high-quality data collection and development of innovative methodologies in analysis. **Joseph F. Fraumeni, Jr., M.D.**, DCEG Director, received an individual award recognizing his contributions to the SEER Program.

"Today, SEER stands as the model and standard of excellence for cancer registries, both on a national and international scale," said Dr. Fraumeni. "Visionary in concept, SEER has earned its name with an unprecedented ability to identify emerging trends, geographic variation, ethnic disparities, and other patterns that have provided new directions for epidemiologic research in cancer etiology and control."

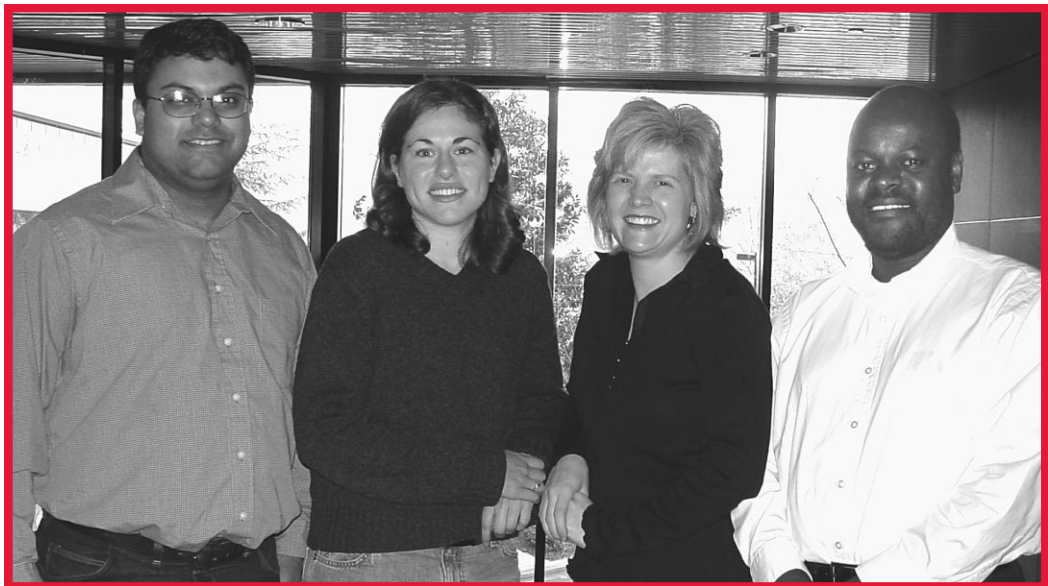
In addition to Dr. Fraumeni's award, DCEG was acknowledged for its contributions to SEER's landmark studies, including the coordination of multicenter case-control studies, the Agricultural Health Study, the study of second cancers, the survey of multiple primary cancers, and the development of cancer mortality maps depicting geographic variation at the county level.

Begun by NCI in January 1973, SEER first collected data on cancer incidence and survival in Connecticut, Iowa, New Mexico, Utah, and Hawaii, and in Detroit and San Francisco-Oakland. The registry gradually expanded to include several other regions of the country. SEER registries routinely collect data on patient demographics, primary tumor site, morphology, stage at diagnosis, first course of treatment, and follow up for vital status from 14 population-based cancer registries and 3 supplemental registries covering approximately 26 percent of the U.S. population. Information on more than 3 million *in situ* and invasive cancer cases is included in the SEER database, and approximately 170,000 new cases are added each year in the SEER coverage areas.

"The recent expansion of SEER has greatly enhanced its value to the research community," said Dr. Robert Croyle, Director of NCI's Division of Cancer Control and Population Sciences, which manages SEER. "Brenda Edwards and her team have done a remarkable job of improving the usability of SEER data and collaborating with DCEG and others to ensure that surveillance data inform both research and policy."

For more information, please visit: *http://seer.cancer.gov/anniversary/*. ■

—Maria Sgambati, M.D.



Former and Current FELCOM Representatives: Abhijit Dasgupta, Margaret Wright, Robin Wilson, Sam Mbulaiteye

NEW REPRESENTATIVES TO NIH FELLOWS COMMITTEE

Robin Wilson, Ph.D., Occupational and Environmental Epidemiology Branch, and **Margaret Wright, Ph.D.**, Nutritional Epidemiology Branch, have been selected as the new DCEG representatives to the NIH Fellows Committee (FELCOM). Dr. Wright will also serve as Chair of the FELCOM mentoring subcommittee. FELCOM is composed of fellows from each NIH Institute and enhances their training experience. Thanks to outgoing FELCOM representatives **Abhijit Dasgupta, Ph.D.** (Biostatistics Branch), and **Sam Mbulaiteye, M.D.** (Viral Epidemiology Branch), for their service on behalf of DCEG, NCI, and NIH. For more information on FELCOM, please visit: *http://felcom.nih.gov*.

SCIENTIFIC HIGHLIGHTS

BRAIN TUMORS

Family History of Cancer and Glioma Risk

Because few studies have examined glioma risk in relation to history of cancer in first-degree relatives, a hospital-based study of glioma cases (n = 489) and controls (n = 799) was conducted. Among participants reporting a family history of brain cancer or a brain tumor, glioma risk was 1.6 (CI = 0.5–5.3; n = 5) and 3.0 (CI = 0.9–10.8; n = 7), respectively, compared with those without such family histories. Increased glioma risk was also observed among subjects reporting a family history of stomach (odds ratio [OR] = 2.2; CI = 1.0–4.6), colon (OR = 1.4; CI = 0.9–2.2), or prostate cancer (OR = 2.1; CI = 1.1–3.8) or Hodgkin's disease (OR = 2.4; CI = 0.9–6.3). **(Hill DA, Inskip PD, Shapiro WR, Selker RG, Fine HA, Black PM, Linet MS. Cancer in first-degree relatives and risk of glioma in adults. *Cancer Epidemiol Biomarkers Prev* 2003;12:1443–1448)**

BREAST CANCER

HER2 Polymorphism Increases Risk of Breast Cancer

The I655V polymorphism in the human epidermal growth factor receptor 2 (*HER2*) proto-oncogene has been associated with an elevated risk of breast cancer in some ethnic groups. Subjects from a community-based study of 5,318 Ashkenazim from the Washington, DC, area were selected for study. The estimated cumulative risk of breast cancer to age 70 was approximately 30 percent higher among *HER2* I655V carriers than noncarriers (RR = 1.33; CI = 1.03–1.83) (Figure 1). The allele's effect was stronger at younger ages (RR = 2.11 for women < 50 years) and especially among younger women with a family history of breast cancer (RR = 8.9). An increased risk of breast cancer associated with the I655V allele was also observed among *BRCA1/2* mutation carriers. The *HER2* valine allele may predispose women to breast cancer, especially young women and women with a positive family history of the disease. **(Rutter JL, Chatterjee N, Wacholder S, Struewing J. The HER2 I655V polymorphism and breast cancer risk in Ashkenazim. *Epidemiology* 2003;14:694–700)**

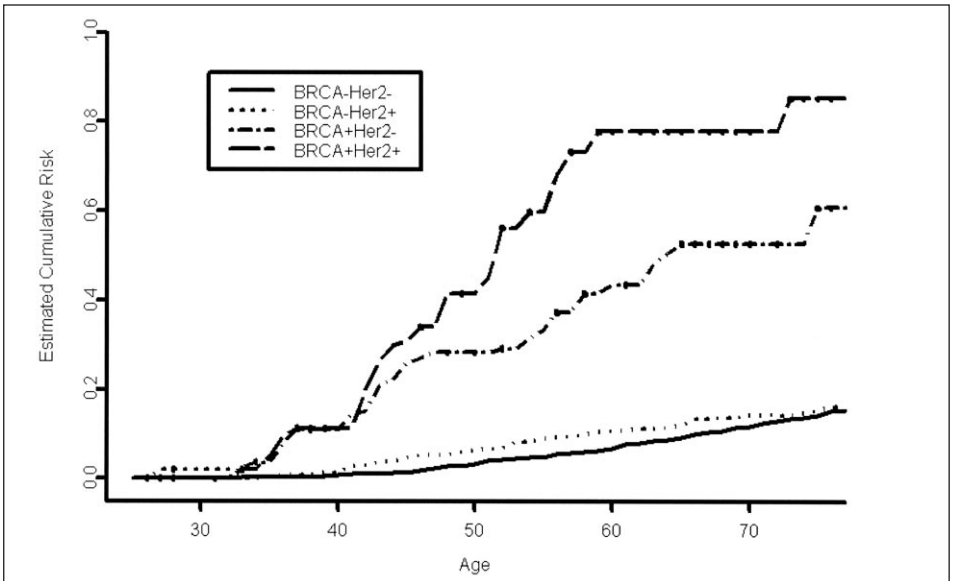


Figure 1. Kin-cohort estimation of breast cancer risk by joint HER2 and BRCA1/2 status in Washington, DC, relatives.

Hormone Levels in Pregnancy

Reductions in breast cancer risk have been reported in daughters of pre-eclamptic pregnancies, suggesting the influence of low *in utero* estrogen concentrations seen in this condition. Levels of estriol, estradiol, estrone, dehydroepiandrosterone, dehydroepiandrosterone-sulfate, androstenedione, and testosterone were measured in mixed umbilical cord sera but were not significantly different in 86 pre-eclamptics compared with 86 uncomplicated pregnancies. Estriol was 9 percent lower ($p = 0.43$) but all the other hormones were actually higher in pre-eclamptics; testosterone and estradiol approached statistical significance ($p = 0.06$ and $p = 0.12$, respectively). These data do not support the hypothesis that the lower breast cancer risk in daughters of pre-eclamptic pregnancies is explained by lower *in utero* estrogen exposure. **(Troisi R, Potischman N, Johnson CN, Roberts JM, Lykins D, Harger G, Markovic N, Siiteri P, Hoover RN. Estrogen and androgen concentrations are not lower in the umbilical cord serum of pre-eclamptic pregnancies. *Cancer Epidemiol Biomarkers Prev* 2003;12:1268–1270)**

CERVICAL CANCER

HPV Variants and Subtypes of Cervical Cancer

Distributions of type-specific human papillomavirus (HPV) variants seen in cervical adenocarcinomas (AC) and squamous cell carcinomas (SCC) are unknown. A total of 85 HPV-16- and/or HPV-18-positive individuals (31 with AC, 43 with SCC, and 11 population controls) were studied because these types are most commonly associated with cervical neoplasia. Cervical AC and SCC differed with respect to the distribution of HPV types and in the intratypic variants observed, with non-European HPV-16 and/or HPV-18 variants more commonly seen in AC. **(Burk RD, Terai M, Gravitt PE, Brinton LA, Kurman RJ, Barnes WA, Greenberg MD, Hadjimichael OC, Fu L, McGowan L, Mortel R, Schwartz PE, Hildesheim A. Distribution of human papillo-**

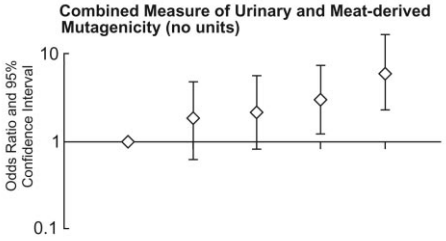


Figure 2. Association between risk for colorectal adenoma and combined urinary and meat-derived mutagenicity.

mavirus types 16 and 18 variants in squamous cell carcinomas and adenocarcinomas of the cervix. *Cancer Res* 2003;63:7215–7220)

COLORECTAL CANCER

Urinary Mutagenicity and Colorectal Adenoma Risk

Urinary mutagenicity and colorectal adenoma risk was investigated in a study of nonsmoking cases (n = 143) and controls (n = 156). Urinary organics were extracted by C18/methanol from overnight urine samples, and mutagenicity was determined in salmonella YG1024 +S9 (Ames test). Adenoma risk was 2.4-fold higher in subjects in the highest versus lowest quintile of urinary mutagenicity (CI = 1.1–5.1). Combining urinary mutagenicity with intake of meat-derived mutagenicity (from an earlier analysis) resulted in a 5.6-fold increase in adenoma risk (CI = 2.2–13.9, highest versus lowest quintile) (Figure 2). Mutagenic exposures from diet may thus contribute to the development of colorectal adenomas. **(Peters U, DeMarini DM, Sinha R, Brooks LR, Warren SH, Chatterjee N, Rothman N. Urinary mutagenicity and colorectal adenoma risk. *Cancer Epidemiol Biomarkers Prev* 2003;12:1253–1256)**

Nitrates and Risk of Colorectal Cancer

Nitrate is a widespread drinking water contaminant, and N-nitroso compound formation may be inhibited by vitamin C and increased by meat intake. In a study of 376 colon cancer cases, 338 rectal cancer cases, and 1,244 controls, only slight increases were associated with measures of nitrate in public water supplies. Subgroup analyses, however, suggested that high levels of nitrate exposure (> 10 years with average nitrate > 5 mg/L) were associated with increased colon cancer risk among those with low vitamin C intake (OR = 2.0; CI = 1.2–3.3) and heavy meat intake (OR = 2.2; CI = 1.4–3.6). **(De Roos AJ, Ward MH, Lynch CF, Cantor KP. Nitrate in public water supplies and the risk of colon and rectum cancers. *Epidemiology* 2003;14:640–649)**

ESOPHAGEAL AND GASTRIC CANCER

Nutritional Factors in Esophageal and Gastric Cancers

Several recent papers reported on results from a randomized nutritional intervention trial in Linxian, China, where rates of esophageal squamous cell cancer and gastric cardia cancer are extremely high. In the first study, the incidence of gastric cardia cancer fell 10 percent for each quartile increase in serum retinol (RR = 0.90; CI = 0.83–0.99) and the incidence of noncardia gastric cancer increased (RR = 1.2 per quartile, CI = 1.0–1.3) with increasing concentration of serum lutein/zeaxanthin. **(Abnet CC, Qiao YL, Dawsey SM, Buckman DW, Yang CS, Blot WJ, Dong ZW, Taylor PR, Mark SD. Prospective study of serum retinol, beta-carotene, beta-cryptoxanthin, and lutein/zeaxanthin and esophageal and gastric cancers in China. *Cancer Causes Control* 2003;14:645–655).**

In the second study, polymorphisms in two genes that code for enzymes that require folate and B-12 as cofactors (methionine synthase reductase [MTRR] A66G and methylenetetrahydrofolate reductase [MTHFR] C677T and A1298C) were studied in relation to these tumors. Individuals with the MTHFR 677TT genotype had higher risks for both tumors combined (RR = 1.45; CI = 1.02–2.05) than those with CC or CT genotypes. Compared with subjects with the MTRR 66AA genotype, those with the AG or GG genotypes had significantly higher risk of esophageal cancer (RR = 1.59; CI = 1.04–2.42). **(Stolzenberg-Solomon RZ, Qiao YL, Abnet CC, Ratnasinghe DL, Dawsey SM, Dong ZW, Taylor PR, Mark SD. Esophageal and gastric cardia cancer risk and folate- and vitamin B(12)-related polymorphisms in Linxian, China. *Cancer Epidemiol Biomarkers Prev* 2003;12:1222–1226)**

In the third study, significant inverse associations were seen between baseline serum selenium and mortality from esophageal cancer (RR = 0.83; CI = 0.71–0.98) and gastric cardia cancer (RR = 0.75; CI = 0.59–0.95). **(Wei WQ, Abnet CC, Qiao YL, Dawsey SM, Dong ZW, Sun XD, Fan JH, Gunter EW, Taylor PR, Mark SD. Prospective study of serum selenium concentrations and esophageal and gastric cardia cancer, heart disease, stroke, and total death. *Am J Clin Nutr* 2004;79:80–85)**

INFECTIOUS AGENTS

No Link Between Simian Virus 40 and AIDS-Associated Lymphoma

Recent studies have reported the detection of DNA sequences from simian virus 40 (SV40) in non-Hodgkin's lymphoma (NHL) associated with acquired immunodeficiency syndrome. To examine this association, data from a cohort study of AIDS patients were analyzed on subjects born in 1958–1961 (putatively exposed to SV40-contaminated poliovirus vaccine as children; n = 39,468) and in 1964–1967 (born after vaccines were cleared of SV40; n = 17,340). Among persons with AIDS, lymphoma incidence was 11.7 versus 10.1 per 1,000 person-years in SV40-exposed versus unexposed individuals, respectively (unadjusted relative risk [RR] = 1.15; CI = 0.99–1.34). After adjustment for race, homosexuality, and age, SV40 exposure was not associated with NHL incidence (RR = 0.97; CI = 0.79–1.20). Childhood exposure to SV40 through receipt of contaminated poliovirus vaccine is not associated with increased risk for AIDS-associated NHL. **(Engels EA, Rodman LH, Frisch M, Goedert JJ, Biggar RJ. Childhood exposure to simian virus 40-contaminated poliovirus vaccine and risk of AIDS-associated non-Hodgkin's lymphoma. *Int J Cancer* 2003;106:283–287)**

Blood Transfusion and Risk of HHV-8 Seroconversion

Human herpesvirus 8 (HHV-8), the etiologic agent for Kaposi's sarcoma, can be detected in peripheral blood, but blood-borne transmission of this virus has not been demonstrated. Children (n = 600) with sickle-cell disease at Mulago Hospital, Kampala, Uganda, were studied to determine if blood transfusions affected HHV-8 seroconversion, as measured by enzyme-linked immunosorbent assays for antibodies against HHV-8 proteins K8.1 and orf 73. HHV-8 antibodies were detected in 117 of 561 (21 percent) children with unambiguous K8.1 results, and seropositivity was more frequent in transfused than never-transfused children (OR = 1.5; CI = 1.0–2.3). Among never-transfused children, HHV-8 seroprevalence increased with age from 7 percent in children aged 0–2 years to 32 percent in those aged 13–16 years (p for trend < .001). Seropositivity increased with the number of reported transfusions, with an overall estimated HHV-8 transmission risk of 2.6 percent per transfusion (Figure 3). In comparison, the annual risk of HHV-8 infection unrelated to transfusion was 2.7 percent. The small risk of HHV-8 transmission by transfusion in Uganda is approximately equivalent to the 1-year cumulative risk of infection from community sources. **(Mbulaiteye SM, Biggar RJ, Bakaki PM, Pfeiffer RM, Whitby D, Owor AM, Katongole-Mbidde E, Goedert JJ, Ndugwa CM, Engels EA. Human herpesvirus 8 infection and transfusion history in children with sickle-cell disease in Uganda. *J Natl Cancer Inst* 2003;95:1330–1335)**

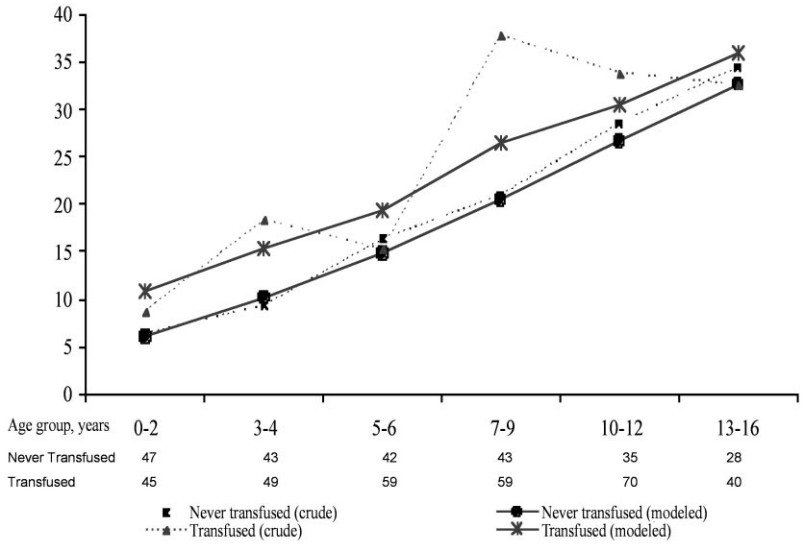


Figure 3. Observed and modeled human herpesvirus 8 (HHV-8) seroprevalence, using K8.1 antibody results, as a function of children's age and transfusion status. The numbers of never transfused and ever transfused children are shown below the graph.

LEUKEMIA

Birth Weight May Contribute to Childhood Leukemia

In a meta-analysis of more than 10,000 children with leukemia from 18 studies, children weighing 4,000 g or more at birth were at higher risk of acute lymphoblastic leukemia (ALL) than children weighing less (OR = 1.3; CI =1.2–1.4). Data were consistent with a dose-response-like effect (OR = 1.1/1,000-gram birth weight increase). These findings emphasize the need for more studies into biologic mechanisms underlying the relation between ALL and high birth weight. **(Hjalgrim LL, Westergaard T, Rostgaard K, Schmiegelow K, Melbye M, Hjalgrim H, Engels EA. Birth weight as a risk factor for childhood leukemia: a meta-analysis of 18 epidemiologic studies. *Am J Epidemiol* 2003;158:724–735)**

Formaldehyde Exposure May Increase Leukemia Risk

Extended follow up on a cohort of 25,619 U.S. industrial workers evaluated the association between measures of formaldehyde exposure (peak exposure, average exposure intensity, cumulative exposure, and exposure duration) and mortality from lymphohematopoietic cancers (n = 178). Compared with workers exposed to low peak levels of formaldehyde (0.1–1.9 ppm), relative risks for myeloid leukemia were 2.43 (CI = 0.81–7.25) and 3.46 (CI = 1.27–9.43) for workers exposed to peak levels of 2.0–3.9 ppm and ≥ 4.0 ppm, respectively (p for trend = 0.009). Compared with workers exposed to low levels of average exposure intensity of formaldehyde (0.1–0.4 ppm), relative risk for myeloid leukemia was 1.15 (CI = 0.41–3.23) and 2.49 (CI = 1.03–6.03) for workers exposed to 0.5–0.9 ppm and ≥ 1.0 ppm average intensity, respectively (p for trend = 0.088). The risks were not associated with cumulative exposure and only weakly with exposure duration. **(Hauptmann M, Lubin JH, Stewart PA, Hayes RB, Blair A. Mortality from lymphohematopoietic malignancies among workers in formaldehyde industries. *J Natl Cancer Inst* 2003;95:1615–1623)**

LIVER CANCER

The Rising Incidence of Liver Cancer in the United States

Data collected by population-based registries of the Surveillance, Epidemiology, and End Results (SEER) program were examined for trends in the incidence of hepatocellular carcinoma. The overall age-adjusted incidence rates of hepatocellular carcinoma increased from 1.4 per 100,000 (1975–77) to 3.0 per 100,000 (1996–1998). Incidence increased 25 percent during 1996–1998 compared with 1993–1995, with the greatest increase in the 45–49-year-old age group. The trends appear tied to the rising prevalence of hepatitis C virus infection acquired during the 1960s and 1970s. **(El-Serag HB, Davila JA, Petersen NJ, McGlynn KA. The continuing increase in the**

incidence of hepatocellular carcinoma in the United States: an update. *Ann Intern Med* 2003;139:817–823)

METHODS

Non-parametric Regression Models for Continuous Exposures

Semiparametric generalized linear models provide a useful extension for estimating relative risks when a study exposure is continuous. The exposure of interest is modeled flexibly using a regression spline or a smoothing spline; other variables are modeled using conventional methods. This approach was applied to case-control data to estimate the dose-response relationship between alcohol consumption and risk of oral cancer among African Americans. A best model was not found but results using linear, cubic, and smoothing splines were consistent in suggesting that there is no risk-free threshold for alcohol consumption. This finding was not apparent using a standard step-function model (Figure 4). In the analysis, the cross-validation curve had global and local minimums. In general, the phenomenon of multiple local minima makes it more difficult to interpret the results and may present a computational roadblock to nonparametric generalized additive models of multiple continuous exposures. (Rosenberg PS, Katki H, Swanson CA, Brown LM, Wacholder S, Hoover RN. Quantifying epidemiologic risk factors using non-parametric regression: model selection remains the greatest challenge. *Stat Med* 2003;22:3369–3381)

Marker Genotypes and Sample Size Calculations

Most sample-size calculations for case-control studies to detect genetic associations with disease have assumed that the disease gene locus is known, whereas, in fact, markers are used. In this study, sample sizes were calculated for unmatched case-control and sibling case-control studies to detect an association between a biallelic marker and a disease governed by a putative biallelic disease locus. Required sample sizes rose with increasing discrepancy between the marker and disease allele frequencies and with less-than-maximal linkage disequilibrium between the marker and disease alleles. Similar results were found for studies of parent-offspring triads based on the transmission disequilibrium test. Other factors influencing sample size were studied, including attributable risk for the disease allele, inheritance mechanism, disease prevalence, and, for sibling case-control designs, extragenetic familial aggregation of disease and recombination. Large sample-size requirements represent a formidable challenge to studies of this type. (Pfeiffer RM, Gail MH. Sample size calculations for population- and family-based case-control association studies on marker genotypes. *Genet Epidemiol* 2003;25:136–148)

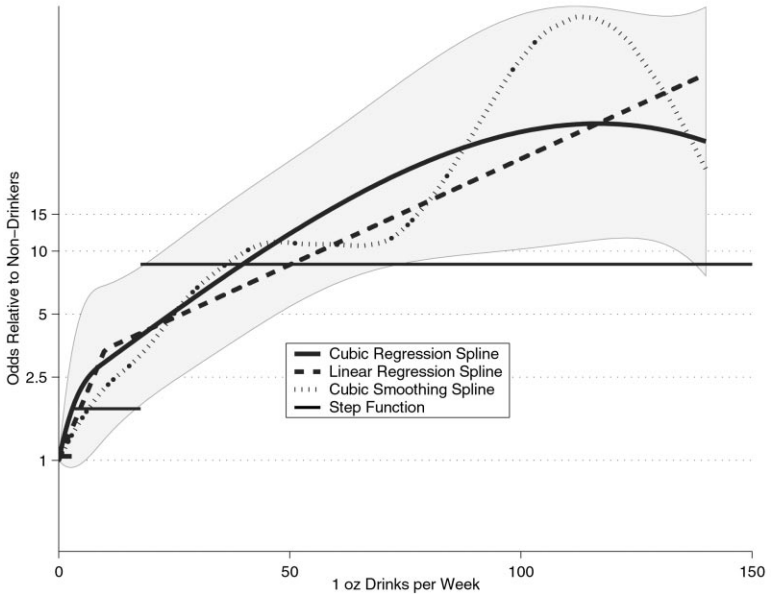


Figure 4. Comparison of estimates of the log odds ratio characterizing alcohol consumption and risk of oral cancer among African Americans. The x-axis shows the number of 1 oz drinks per week, and the y-axis shows the odds ratio for each value of drinks per week relative to non-drinkers on a logarithmic scale. Curves are shown for the best-fitting linear and cubic regression splines selected by Akaike information criterion, the best-fitting cubic smoothing spline selected by generalized cross-validation, and a standard step function model with three steps and a reference category of zero. Confidence intervals are shown for the cubic regression spline.

Adjustment for Competing Risk in Kin-Cohort Estimation

Kin-cohort design can be used to study the effect of a genetic mutation on the risk of multiple events using the same study. Existing methods for kin-cohort estimation allow estimation of the risk of one event at a time, with the assumption that censoring events are unrelated to the genetic mutation under study. These methods, however, may produce biased estimates of risk when multiple events are related to the genetic mutation, and follow up of events may be censored by the onset of other events. A competing risk framework was used to address this problem and to show that cause-specific hazard functions for carriers and noncarriers are identifiable from kin-cohort data. A demonstration of the proposed method is used to estimate the risk of ovarian cancer from *BRCA1/2* mutations in the absence of breast cancer, based on data from the Washington Ashkenazi kin-cohort study. (Chatterjee N, Hartge P, Wacholder S. Adjustment for competing risk in kin-cohort estimation. *Genet Epidemiol* 2003;25:303–313)

Comparison of DNA Quantification Methods

The accuracy and precision of DNA concentration estimates are critical factors for efficient use of DNA samples in high-throughput genotype and sequence analyses. Spectrophotometric/optical density (OD) DNA quantification was compared to

two fluoro- metric quantification methods, the PicoGreen® assay (PG) and a novel real-time quantitative genomic PCR assay specific to a region at the human *BRCA1* locus using 22 lymphoblastoid cell line DNA samples. Among the three methods evaluated, OD was the DNA quantification method most concordant with the reference sample. A large fraction of the total variance for all three methods (36.0–95.7 percent) was explained by sample-to-sample variation, whereas the amount of variance attributable to sample handling was small (0.8–17.5 percent). Residual error (3.2–59.4 percent), corresponding to unmodeled factors, contributed a greater extent to the total variation than did the sample-handling procedures. **(Haque KA, Pfeiffer RM, Beerman MB, Struewing JP, Chanock SJ, Bergen AW. Performance of high-throughput DNA quantification methods. *BMC Biotechnol* 2003;3:1–10)**

Comparison of Dietary Assessment Methods

Several biomarker studies have cast doubt on whether the food frequency questionnaire (FFQ) has sufficient precision to allow detection of diet–disease associations. Data from the Observing Protein and Energy Nutrition (OPEN) study were used to compare the FFQ to the 24-hour recall (24HR). Participants (261 men and 223 women) completed FFQs and 24HRs on two occasions 3 months apart, and a doubly labeled water assessment and two 24-hour urine collections during the 2 weeks after the first FFQ and 24HR assessment. For absolute energy and protein, a single FFQ attenuation factor is 0.04–0.16 and repeat administrations lead to little improvement (0.08–0.19). Attenuation factors for a single 24HR are 0.10–0.20 but four repeats would yield attenuations of 0.20–0.37. For protein density, a single FFQ has an attenuation of 0.3–0.4; for a single 24HR the attenuation factor is 0.15–0.25 but would increase to 0.35–0.50 with four repeats. Because of severe attenuation, the FFQ cannot be recommended for evaluating disease risks associated with absolute intake of energy or protein. Although this attenuation is lessened in analyses of energy-adjusted protein, it is substantial for the FFQ and multiple 24HR. The utility of either instrument for detecting important but moderate relative risks (between 1.5 and 2.0), even for energy-adjusted dietary factors, is questionable. **(Schatzkin A, Kipnis V, Carroll RJ, Midthune D, Subar AF, Bingham S, Schoeller DA, Troiano RP, Freedman LS. Comparison of a food frequency questionnaire with a 24-hour recall for use in an epidemiological cohort study: results from the biomarker-based Observing Protein and Energy Nutrition (OPEN) study. *Int J Epidemiol* 2003; 32:1054–1062)**

YALE UNIVERSITY AWARDED FIRST TRAINING GRANT

Yale University was awarded the first NCI Graduate Partnership Program TU2 training grant in Cancer Epidemiology and Genetics. DCEG will partner with Yale's Department of Epidemiology and Public Health to develop the training program, which supports tuition and dissertation research by predoctoral students training in the epidemiology of nutritional, environmental, and occupational determinants of cancer. The partnership will include coursework at Yale coupled with summer training at NCI. Once coursework is complete, dissertation research will be conducted at NCI under the guidance of DCEG and Yale investigators, and Yale will award the doctoral degree.

At NCI, **Demetrius Albanes, M.D.**, leads the partnership as head of the DCEG Office of Education, assisted by steering committee members **Aaron Blair, Ph.D.**, Chief of the Occupational and Environmental Epidemiology Branch, and **Arthur Schatzkin, M.D., Dr.P.H.**, Chief of the Nutritional Epidemiology Branch. At Yale, Dr. Susan Mayne, Associate Professor of epidemiology and public health, serves as principal investigator for the grant. Interested students may contact Dr. Albanes at daa@nih.gov or phone 301-594-2869, or Dr. Mayne at susan.mayne@yale.edu or phone 203-785-6274.

NASOPHARYNGEAL CANCER

Polymorphisms in DNA Repair Genes Alter Risk of NPC

A case-control study of 334 patients with nasopharyngeal carcinoma (NPC) and 283 controls was conducted to investigate whether polymorphisms of DNA repair genes hOGG1 and XRCC1 mediated NPC risk in a high-risk area in Taiwan. Among subjects with putative high-risk genotypes for hOGG1 and XRCC1, the odds ratio was 3.0 (CI = 1.0–8.8). Among subjects who also had a polymorphism of CYP2E1, which metabolizes dietary nitrosamines, the odds ratio rose to 25 (CI = 3.5–177). **(Cho EY, Hildesheim A, Chen CJ, Hsu MM, Chen IH, Mittl BF, Levine PH, Liu MY, Chen JY, Brinton LA, Cheng YJ, Yang CS. Nasopharyngeal carcinoma and genetic polymorphisms of DNA repair enzymes XRCC1 and hOGG1. *Cancer Epidemiol Biomarkers Prev* 2003;12:1100–1104)**

PROSTATE CANCER

BPH Treatment Affects Subsequent Cancer Risk

To investigate whether men with benign prostatic hyperplasia (BPH) may have an increased risk of prostate cancer, record-linkage data from 86,626 men in a Swedish population-based study were used to assess prostate cancer risk up to 26 years after the BPH diagnosis. Subjects with BPH experienced a 2 percent excess incidence of prostate cancer after 10 years of follow up, but the patterns were influenced by BPH treatment type. Men who underwent a transvesicular adenomectomy had 22 percent lower incidence and 23 percent lower mortality from prostate cancer after the first 5 years of follow up; those with transurethral resection had 10 percent higher incidence but 17 percent lower mortality. In contrast, BPH patients who did not receive surgical intervention experienced significant excesses in incidence (18 percent) and

mortality (77 percent) from prostate cancer. Further studies are needed to confirm the small excess risk of prostate cancer among BPH patients and the putative impact of treatment methods on subsequent risk. **(Chokkalingam AP, Nyren O, Johansson JE, Gridley G, McLaughlin JK, Adami HO, Hsing AW. Prostate carcinoma risk subsequent to diagnosis of benign prostatic hyperplasia: a population-based cohort study in Sweden. *Cancer* 2003;98:1727–1734)**

Mutations in *BRCA1/2* Increase Risk of Prostate Cancer

To estimate the risk of prostate cancer associated with the common Ashkenazi founder mutations of the *BRCA1* and *BRCA2* genes, 979 Ashkenazi Jewish men diagnosed with prostate cancer in Israel were studied. DNA was tested for the three founder mutations in 940 cases, and a mutation was identified in 3.2 percent (30/940), representing a 2-fold increase compared with a referent group of Ashkenazi men over 50 years old with no history of prostate cancer (OR = 2.1; CI = 1.2–3.6). No difference was found in the mean age at diagnosis between cases with and without a founder mutation. No histologic differences were observed between BRCA-associated prostate cancer cases and noncarrier prostate cancer cases. **(Giusti RM, Rutter JL, Duray PH, Freedman LS, Konichezky M, Fisher-Fischbein J, Greene MH, Maslansky B, Fischbein A, Gruber SB, Rennert G, Ronchetti RD, Hewitt SM, Struewing JP, and Iscovich J. A twofold increase in BRCA mutation related prostate cancer among Ashkenazi Israelis is not associated with distinctive histopathology. *J Med Genet* 2003;40:787–792)**

RADIATION

Low Doses of Ionizing Radiation and Cancer Risk

DCEG staff participated in an international collaborative effort to evaluate the carcinogenic effects of low-level exposure to ionizing radiation. The effects of low-dose radiation are of societal importance in relation to issues as varied as cancer screening tests, the future of nuclear power, occupational radiation exposure, frequent-flyer risks, manned space exploration, and radiological terrorism. There are two overarching questions in quantifying low-dose radiation risks. First, what is the lowest dose of x or gamma radiation for which good evidence exists of increased cancer risks in humans? Epidemiological data suggest that it is approximately 10–50 mSv for an acute exposure and 50–100 mSv for a protracted exposure. Second, what is the most appropriate way to extrapolate such cancer risk estimates to still lower doses? A linear extrapolation of cancer risks from intermediate to very low doses appears to be the most appropriate methodology, although this approach is not necessarily the most conservative and will likely result in an underestimate of some radiation-induced cancer risks and an overestimate of others. **(Brenner DJ, Doll R, Goodhead DT, Hall EJ, Land CE, Little JB, Lubin JH, Preston DL, Preston RJ, Puskin JS, Ron E, Sachs RK, Samet JM, Setlow RB, Zaider M. Cancer risks attributable to low doses of ionizing radiation: Assessing what we really know. *Proc Natl Acad Sci* 2003;100:13761–13766)**

Exposure to Thorotrast and Cancer Risk

Patients injected with Thorotrast (thorium-232) during radiographic procedures, beginning in the 1930s, experienced long-term internal exposure to alpha-particle-emitting radionuclides. Site-specific cancer incidence and mortality was evaluated in an international cohort of 3,042 patients injected during cerebral angiography with either Thorotrast (n = 1,650) or nonradioactive agents (n = 1,392). Compared with nonexposed patients, significantly increased risks in Thorotrast patients were observed for all incident cancers combined (RR = 3.4, CI = 2.9–4.1, n = 480, Denmark and Sweden) and for cancer mortality (RR = 4.0, CI = 2.5–6.7, n = 114, United States). Approximately 335 incident cancers were above expectation, with large excesses seen for cancers of the liver, bile ducts, and gallbladder (55 percent excess cancers) and leukemias other than chronic lymphocytic leukemia (8 percent excess cancers). The RR of all incident cancers increased with time since angiography ($p < 0.001$) and was 3-fold at 40 or more years; significant excesses (standardized incidence ratio = 4.0) persisted for 50 years. Increasing cumulative dose of radiation was associated with an increasing cancer incidence and mortality, especially for cancers of the liver and biliary tract. **(Travis LB, Hauptmann M, Gaul LK, Storm HH, Goldman MB, Nyberg U, Berger E, Janower ML, Hall P, Monson RR, Holm LE, Land CE, Schottenfeld D, Boice JD Jr, Andersson M. Site-specific cancer incidence and mortality after cerebral angiography with radioactive thorotrast. *Radiat Res* 2003; 160:691–706)**

UTERINE CANCER

Tamoxifen and Risk of Rare Endometrial Cancers

Recent studies suggest that the tamoxifen-related risk of uterine corpus cancer may be especially high for some uncommon cell types, although the magnitude of risk has not been quantified. Data from 39,451 breast cancer patients initially treated with tamoxifen was evaluated. The overall risk of subsequent uterine corpus cancer was increased more than 2-fold (observed-to-expected ratio [O/E] = 2.17, CI = 1.95–2.41) relative to the general SEER population. Relative risk was substantially higher for malignant mixed mullerian tumors (MMMTs) (O/E = 4.62) than for endometrial adenocarcinomas (O/E = 2.07), although excess absolute risk was another 1.4 versus 8.4 cancers per 10,000 women per year, respectively. Among women who survived for 5 years or longer, there was an 8-fold relative risk for MMMTs and a 2.3-fold risk for endometrial adenocarcinomas, with those developing MMMTs having a worse prognosis. These findings indicate that tamoxifen may have delayed effects, such as the increased risk of MMMTs, rare but aggressive tumors of unclear pathogenesis. **(Curtis RE, Freedman DM, Sherman ME, Fraumeni JF Jr. Risk of malignant mixed mullerian tumors after tamoxifen therapy for breast cancer. *J Natl Cancer Inst* 2004;96:70–74)**

DCEG PEOPLE IN THE NEWS

Michael Alavanja, Ph.D., Occupational and Environmental Epidemiology Branch (OEEB), spoke on "Cancer incidence in the Agricultural Health Study cohort" at the International Society of Environmental Epidemiology meeting in Perth, Australia, last September.


Andrea Baccarelli

Andrea Baccarelli, M.D., Ph.D., Genetic Epidemiology Branch (GEB), received his doctoral degree in Occupational and Environmental Health from the University of Milan, Italy, last November. Dr. Baccarelli's dissertation project, "The aryl-hydrocarbon receptor pathway and dioxin toxic effects in humans: Molecular epidemiology investigations on the Seveso population," was based on research conducted at DCEG in collaboration with **Maria Teresa Landi, M.D., Ph.D.** (GEB). Dr. Baccarelli is leaving DCEG to become Assistant Professor in the Department of Occupational and Environmental Health at the University of Milan, Italy.


Andre Bouville

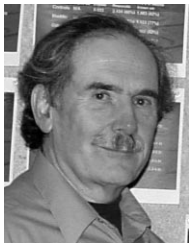
Andre Bouville, Ph.D., Radiation Epidemiology Branch (REB), has been designated a National Associate by the National Academies. This lifetime honor is given in recognition of extraordinary service to the National Academies, which serve as advisor to the nation in matters of science, engineering, and health. Over the past 10 years, Dr. Bouville has made significant contributions to the National Research Council in evaluating health effects from radioactive fallout. Dr. Bouville also received the Presidential Rank Award, a prestigious honor given to senior career government employees with a sustained record of professional and/or scientific achievement that is recognized at national and international levels.


Louise Brinton

Louise Brinton, Ph.D., Hormonal and Reproductive Epidemiology Branch (HREB), spoke on "Causes of infertility and ovarian cancer risk" at the annual meeting of the American Society of Reproductive Medicine in October in San Antonio, TX.


Linda Morris Brown

Linda Morris Brown, Dr.P.H., Biostatistics Branch (BB), chaired the Medical Service Corps Section at the annual meeting of the Association of Military Surgeons of the United States, held in November in San Antonio.


Kenneth Cantor

Kenneth Cantor, Ph.D. (OEEB), spoke on "Non-Hodgkin's lymphoma and the agricultural environment" at a meeting on Exploring Environmental Links to Disease held in December in Sioux Falls, SD.

Philip Castle, Ph.D., M.P.H. (HREB), gave a talk in September on "Cervical cancer risk factors and human papillomavirus (HPV) vaccines" at the Latin American Federation of Oncology Societies Symposia on Cervical Cancer, in Córdoba, Argentina.

Wong-Ho Chow, Ph.D. (OEEB), spoke on the epidemiology of renal cancer at the Society of Urologic Oncology meeting held in Bethesda, MD, last December; **Lee Moore, Ph.D.** (OEEB), spoke on the epidemiology of bladder cancer at the same meeting.


Amanda Cross

Amanda Cross, Ph.D., a postdoctoral fellow in the Nutritional Epidemiology Branch (NEB), received a Scholar-in-Training travel award from the Molecular Epidemiology Group of the American Association for Cancer Research (AACR). Dr. Cross was recognized for her study, "Heterocyclic amines formed in meat cooked at high temperatures may increase prostate cancer risk," based on data from the Prostate, Lung, Colorectal, and Ovarian Cancer (PLCO) Study.


Susan Devesa

Susan Devesa, Ph.D. (BB), spoke on "International lung cancer trends by histologic type" at the AACR Frontiers in Cancer Prevention Research meeting in Phoenix, AZ, last October.


Eric Engels

Eric Engels, M.D., Viral Epidemiology Branch (VEB), spoke on "Epidemiology of cancer in persons with HIV/AIDS" at the NCI Meeting on the Clinical Research Agenda for AIDS Malignancies in Bethesda, MD, last September.

James Goedert, M.D. (VEB), spoke on "Overview on the infectious causes of cancer" and "Kaposi sarcoma and other cancers associated with HIV/AIDS and Kaposi Sarcoma Herpes Virus (KSHV)" at the American Society of Clinical Oncology "Meet the Experts" session for journalists in New York City last December. At the same meeting, **Charles Rabkin, M.D.** (VEB), spoke on "Helicobacter pylori and gastric cancer."


Mark Greene

Mark H. Greene, M.D., Clinical Genetics Branch (CGB), spoke on "Surgical risk reduction and ovarian screening in the management of women at increased genetic risk of ovarian cancer" at the McGee Women's Hospital in Pittsburgh, PA, in September, and at Case-Western Reserve Cancer Center in Cleveland, OH, in November.


Michie Hisada

Michie Hisada, M.D., Sc.D., Ph.D. (VEB), spoke on "A persistent paradox of HTLV-I natural history: Parallel analyses of Japanese and Jamaican carriers" at a Cancer Prevention Seminar given by the Department of Epidemiology, Harvard School of Public Health, last December.


Ann Hsing

In October, **Ann Hsing, Ph.D.** (HREB), served as a member of the Scientific Advisory Committee to the Center for Prostate Disease Research (CPDR) at the Department of Defense. In December, Dr. Hsing was promoted to the rank of full professor in the Department of Epidemiology and Biostatistics, School of Public Health and Health Services, and the Department of Urology, School of Medicine and Health Sciences, at the George Washington University, where she is an adjunct faculty member.


Peter Inskip

Peter Inskip, Sc.D. (REB), spoke on "Etiology of brain tumors: role of endogenous vs. exogenous factors" and "Multiple primary cancers involving cancer of the brain or central nervous system" in November at the annual meeting of the Society for Neuro-Oncology in Keystone, CO.


James Lacey

In October, **James Lacey, Ph.D, M.P.H.** (HREB), participated in "Ovarian cancer research at NCI," a presentation to U.S. Congressman Rodney Freylinghausen (R-NJ) and constituents who are members of Kaleidoscope of Hope, an ovarian cancer patient and survivor group. Dr. Lacey spoke on "The epidemiology of ovarian cancer: DCEG's approach to a challenging disease."


Michael Leitzmann

Michael Leitzmann, Ph.D. (NEB), spoke on "Obesity, energy balance, and cancer risk" at the International Agency for Research on Cancer (IARC) and at George Washington University.


Unhee Lim

Unhee Lim, Ph.D. (NEB), received an AFLAC Scholar-in-Training Award to attend the AACR Frontiers in Cancer Prevention Research meeting last October in Phoenix, AZ. Dr. Lee won the award for her abstract on "Dietary B vitamins and the risk of lymphoid cancers in male smokers."


International Familial Chronic Lymphocytic Leukemia Consortium

Neil Caporaso, M.D., and **Lynn Goldin, Ph.D.** (GEB), organized the second meeting of the International Familial Chronic Lymphocytic (CLL) Consortium, held in October during the 10th International Workshop on CLL in Stresa, Italy. At the meeting, Dr. Caporaso spoke on "What do we understand from familial CLL," and Dr. Goldin spoke on "Familial risk of lymphoproliferative tumors in families of patients with CLL: Results from the Swedish family cancer database." Drs. Caporaso and Goldin were also invited to the Mayo Clinic last December to speak on the genetics of familial CLL.


Roxana Moslehi

Roxana Moslehi, Ph.D. (GEB), gave invited presentations last October on cancer risks associated with DNA repair genes at the Graduate School of Public Health at the University of Pittsburgh and at the Georgetown University Lombardi Cancer Center.

Dilys Parry, Ph.D. (GEB), was appointed Vice-Chair of the NCI Special Studies Institutional Review Board (IRB). Dr. Parry has served on the IRB since 1995. **Michael Alavanja, Ph.D.** (OEEB), will join the IRB as a new member.


Ulrike Peters

Ulrike Peters, Ph.D. (NEB), spoke on the relation of diet to colorectal adenoma based on data from the PLCO study at M.D. Anderson Cancer Center in October.


Charles Rabkin

Charles Rabkin, M.D. (VEB), gave a talk on "The molecular epidemiology of AIDS-related cancers" at Ernst-Moritz-Arndt University in Greifswald, Germany, last November.

REB scientists **Elaine Ron, Ph.D.,** and **Andre Bouville, Ph.D.,** served as Chair and Executive Secretary, respectively, of the second international Chornobyl thyroid cancer working group held in Geneva last December. **Maureen Hatch, Ph.D.,** and **Ihor Masnyk, Ph.D.** (REB), also participated. The working group aims to improve the quality of data in all Chornobyl-related studies of thyroid disease. Drs. Bouville, Hatch, and Ron also served as expert advisors to the Chornobyl Forum, a group formed in 2003 to communicate objective, scientifically sound information about the health effects of the nuclear accident. The Forum's first meeting, which explored the current scientific assessment of thyroid disease risk in children and adults exposed to radiation, was held at the World Health Organization in Geneva, Switzerland, last December.


Nathaniel Rothman

Nathaniel Rothman, M.D., M.P.H., M.H.S. (OEEB), gave an invited presentation on "Human genome epidemiology" at the Korean National Cancer Prevention Center, Seoul, Korea, last December.


Arthur Schatzkin

Arthur Schatzkin, M.D., Dr.P.H. (NEB), delivered a plenary session on "Strength of the evidence underlying modifiable causes of cancer-diet" at the AACR Frontiers in Cancer Prevention Research meeting in Phoenix, AZ, last October. Dr. Schatzkin also gave an invited presentation on diet and cancer at the University of Arizona Cancer Center.


Rashmi Sinha

Rashmi Sinha, Ph.D. (NEB), was selected as a Sigma Xi Distinguished Lecturer for 2004–2005. Sigma Xi is a scientific research society with a membership of more than 70,000 scientists and engineers who are elected based on their research achievements.

Patricia Stewart, Ph.D. (OEEB), gave three invited presentations at Central Missouri State University last October on a variety of topics, including managing complex occupational safety and health studies and exposure assessment for epidemiologic research.

Margaret Tucker, M.D. (GEB), gave an invited talk on "Risk factors for cutaneous malignant melanoma" at the 3rd Euroskin Conference in Stockholm, Sweden, last September. Dr. Tucker also spoke on "Genetic epidemiology of melanoma" at the All Ireland Cancer Conference, in Cork, Ireland, last October, and on "Genetic susceptibility and risk of melanoma" at the Perspectives in Melanoma VI meeting in Miami, FL, last November.


Roel Vermeulen

Roel Vermeulen, Ph.D. (OEEB), gave invited talks on "Exposure assessment in occupational epidemiology" and "Data-driven exposure assessment" at the International Symposium on Evaluation of Occupational Exposures to Carcinogens last October in Sao Paolo, Brazil.


Sholom Wacholder

Sholom Wacholder, Ph.D. (BB), gave talks on false-positive and false-negative findings in molecular epidemiology studies at a special AACR Conference on "Single nucleotide polymorphisms, haplotypes, and cancer" in September; at the 6th International Meeting on Single Nucleotide Polymorphism and Complex Genome Analysis in November; and at the NIH Research Festival in October. Dr. Wacholder also spoke on "Molecular epidemiology studies: Do the old control selection rules still apply?" at the Albert Einstein College of Medicine.

COMINGS…GOINGS


Kenneth Adams

Kenneth Adams, Ph.D., has joined the Nutritional Epidemiology Branch (NEB) as a postdoctoral fellow. Dr. Adams earned his Ph.D. in epidemiology at the University of Washington in Seattle in 2003. His dissertation research, conducted at the Fred Hutchinson Cancer Research Center, addressed whether soy isoflavones altered serum and tissue biological markers in a randomized intervention trial. In DCEG, he will study links between energy balance and cancer and the mechanisms by which obesity and physical activity affect the risk of various cancers, including alterations of circulating growth factors and cytokines.


Bryce Baker

Bryce Baker has joined the DCEG Administrative Resource Center (ARC) as an administrative technician. Mr. Baker graduated in 2000 from Western Maryland College, where he studied communications, elementary education, and studio art. Before joining NCI, he worked in marketing and advertising for two educational software companies. As administrative assistant he will handle a variety of tasks, including travel orders and personnel actions. Mr. Baker is the fourth member of his family to work at NIH.


Laura Beane-Freeman

Laura Beane-Freeman, Ph.D., has joined the Occupational and Environmental Epidemiology Branch (OEEB) for her preceptorship as part of the DCP Cancer Prevention Fellowship Program. Dr. Beane-Freeman received a B.S. in biology from Iowa State University and a Ph.D. in epidemiology from the University of Iowa. Her dissertation dealt with arsenic exposure, artificial tanning, and melanoma risk. While in DCEG, Dr. Beane-Freeman plans to broaden her experience in assessing the carcinogenic risks of environmental and occupational exposures and gene-environment interactions using large-scale population epidemiologic studies, including the Shanghai women's cohort.


Sonja Berndt

Sonja Berndt, Pharm.D., has joined OEEB as a doctoral student in the Department of Epidemiology at the Johns Hopkins Bloomberg School of Public Health. Dr. Berndt received a B.A. in English literature from Dartmouth College in 1994 and a Doctor of Pharmacy degree from the University of Michigan in 1999. She will conduct research for her dissertation using data from the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer cohort study.

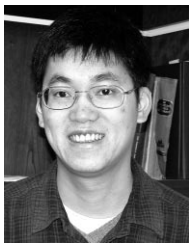

Raymond Carroll

Raymond Carroll, Ph.D., will be a visiting scientist in the Biostatistics Branch (BB) through June 2004. Dr. Carroll is the Texas A & M University Distinguished Professor of Statistics, Nutrition, and Toxicology, and is an expert on the theory of statistics and its applications to problems of missing data and covariate measurement errors in epidemiology.

Elizabeth Challenor-Reese recently left HREB to accept a position in the Division of Epidemiology and Clinical Applications at the National Heart, Lung and Blood Institute.


Patricia Chandler

Patricia Chandler joined the Office of Division Operations and Analysis (ODOA) as an epidemiology program assistant last October. Ms. Chandler previously worked in the Maternal and Child Health Bureau of the Health Resources and Services Administration as administrative assistant to the Deputy Director. She began her career at NIH in 1998 as an intern in NCI's Support Staff Training and Retention program and later joined the Office of the Director (OD) of the Division of Clinical Sciences under Dr. Edison Liu. After the Center for Cancer Research was established in 2000, she continued working in the OD with Drs. J. Carl Barrett and Kathryn Zoon, managing numerous administrative tasks.


Eric Chen

Eric Chen, Ph.D. (BB), has joined DCEG as a postdoctoral fellow. Dr. Chen received his doctoral degree in biostatistics from the University of Waterloo in October 2003. His thesis, "Methods for the Analysis of Interval-Censored Multi-Type Event History Data," was recognized with the Ph.D. Comprehensive Award and the D.A. Sprott Award for best thesis proposal in a calendar year. At DCEG, Dr. Chen will continue his research in survival analysis and is working with Dr. Philip S. Rosenberg to develop methods for tackling multiple-comparison problems in

genetic association studies based on large-scale analyses of single nucleotide polymorphisms and haplotypes.


Sarah Daugherty

Sarah Daugherty, M.P.H., has joined OEEB as a predoctoral fellow. Ms. Daugherty received a B.A. from Carleton College and a dual M.P.H. in epidemiology and health behavior/health education at the University of Michigan. Before beginning her doctoral work at Johns Hopkins Bloomberg School of Public Health, she worked at the Research Triangle Institute in the health and social policy division. While at DCEG, she will carry out a project on genetic variants in prostate cancer and colorectal adenomas.


Neelam Giri

Neelam Giri, M.D., has joined the Clinical Genetics Branch (CGB) as a staff clinician. Dr. Giri received a medical degree from the University of Bombay, India, and trained as a pediatrician and pediatric hematologist/oncologist in Sydney, Australia; New York Medical College; and the NCI Pediatric Oncology Branch. Before joining NCI, she was a staff physician in blood and bone marrow transplantation at the Alfred I. duPont Hospital for Children in Wilmington, DE. Dr. Giri will work with Dr. Blanche Alter on a study of cancer susceptibility in inherited bone marrow failure syndromes.


Marc Gunter

Marc Gunter, Ph.D., has joined the Nutritional Epidemiology Branch (NEB) as a postdoctoral fellow. Dr. Gunter received a Ph.D. in molecular biology from the University of Cambridge in 2002. His doctoral work explored the relationship between inherited variation in carcinogen metabolism and colorectal neoplasia risk among participants of the U.K. Flexible Sigmoidoscopy Screening Trial and European Prospective Investigation into Cancer study. During his fellowship, Dr. Gunter will focus on gene–diet interactions in the framework of large epidemiologic studies.

INDIA HEALTH STUDY MEETING TAKES PLACE

Last September, NEB researchers **Tanuja Rastogi, Ph.D.**, **Arthur Schatzkin, M.D., Dr.P.H.**, and **Rashmi Sinha, Ph.D.**, organized and hosted the India Health Study and Rare Cancers in India Meeting in Rockville, MD. Approximately 30 scientists from India, NCI, and other U.S. institutions were invited to discuss issues related to implementing the India Health Pilot Study. The study aims to elucidate dietary patterns and other lifestyle risk factors in relationship to cancer risk. Topics included endpoint ascertainment, strengths and weaknesses of different Indian registries, details of study questionnaires, and biological sampling and analysis issues. The India Health Pilot Study steering committee includes **Sholom Wacholder, Ph.D.** (BB), and Drs. John Potter (University of Washington), Elio Riboli and Rengaswamy Shankarnarayanan (International Agency for Research on Cancer), and Walter Willett (Harvard School of Public Health). The rare cancers portion of the meeting provided an overview of current cancer epidemiology in India. The meeting was partly funded by the NIH Office for Rare Diseases.


India Health Study: R. Samavedam, B. Rajan, U. Chattopadhyay, R. Sinha, N. Kumar, K. Verma, S. Shastri, T. Rastogi, B. Yeole, A. Mathews, S. Goenka


Timothy Jorgensen

Timothy J. Jorgensen, Ph.D., M.S., will spend a sabbatical year in the Radiation Epidemiology Branch (REB). Dr. Jorgensen, an associate professor in the Department of Radiation Medicine at the Georgetown University Lombardi Cancer Center, is completing an M.P.H. at the Johns Hopkins University. His research focuses on mechanisms of radiation-induced signal transduction and DNA repair, and identifying molecular targets for sensitizing tumors to radiotherapy. Dr. Jorgensen recently received NCI's Ruth L. Kirschstein Senior Fellow Award for his project on "DNA Repair Gene Polymorphisms and Breast Cancer Risk."


Melinda Butsch Kovacic

Melinda Butsch Kovacic, Ph.D., M.P.H., recently joined HREB through the DCP Cancer Prevention Fellowship Program. She received a Ph.D. in biochemistry from Ohio State University and an M.P.H. degree from Harvard University. She will work with Dr. Allan Hildesheim (HREB) on analyzing immunologic factors related to human HPV persistence and progression.

Victor Kryuchov, Ph.D., visited the Chornobyl Research Unit (REB), in November. Dr. Kryuchov, who comes from the Institute of Biophysics in Moscow, Russia, worked with Drs. Andre Bouville and Nickolas Luckyanov on projects related to the dose reconstruction method RADRUE (radiation dose reconstruction with uncertainty estimates) and its use in the study of Chornobyl clean-up workers.

Dale Preston, Ph.D., Chief of the Department of Statistics at the Radiation Effects Research Foundation, in Hiroshima, Japan, visited the REB in October to work with Drs. Charles Land, Kiyohiko Mabuchi, and Elaine Ron on studies of cancer among atomic bomb survivors.


Lynn Rundhaugen

Lynn Rundhaugen has joined the DCEG OD as a communications fellow. Ms. Rundhaugen holds bachelor's degrees in biology and economics from St. Olaf College and Northwestern University, respectively. She is an M.P.H. candidate at Northwestern University and, as part of her graduate program, Ms. Rundhaugen studied international health and social policy in Norway, Ireland, and Germany. Before arriving at NIH, Ms. Rundhaugen worked at the Robert H. Lurie Comprehensive Cancer Center of Northwestern University, first as a laboratory technician and most recently as a Certified Clinical Research Coordinator, working closely with the leukemia program. During her 6-month fellowship in DCEG, Ms. Rundhaugen will assist with communications projects.


Min Shen

Min Shen, M.D., Ph.D., has joined OEEB as a postdoctoral fellow. Dr. Shen received a medical degree and a doctorate in epidemiology from Tongji Medical College in China. Before coming to NCI, he worked at the International Agency for Research on Cancer in studies of gene-environment interactions in the development of bladder cancer. At DCEG, Dr. Shen will collaborate on a study of lung cancer among benzene-exposed workers in China.


Honghong Zhu

Honghong Zhu, M.D., M.S., a doctoral student in the Department of Epidemiology at the Johns Hopkins Bloomberg School of Public Health, has joined OEEB as a predoctoral fellow. Dr. Zhu received a medical degree from Zhejiang Medical University, China, in 1992 and a master's degree in environmental toxicology and microbiology from Clemson University in 2003. She will conduct research for her dissertation using the Shanghai women's cohort study.

ERRATUM

In the November 2003 issue, we mistakenly identified Bonnie Pedersen, a 2003 summer intern in VEB, as **Consol Serra Pujadas, M.D., Ph.D.**, who was a visiting scientist in the OEEB last summer.


Bonnie Pedersen

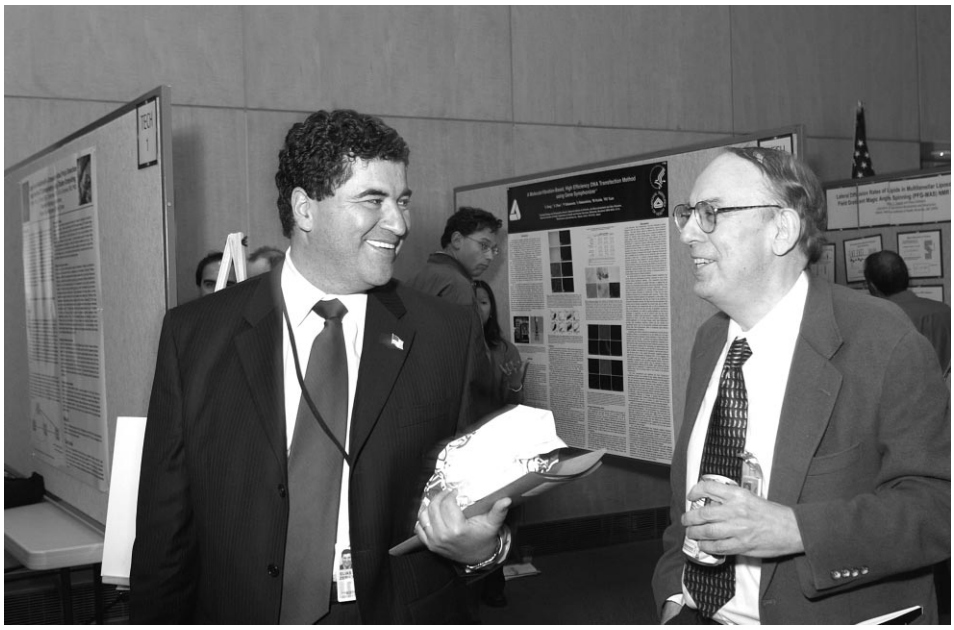

Consol Serra Pujadas

EPIDEMIOLOGY FEATURED AT NIH RESEARCH FESTIVAL

More than 50 DCEG scientists took part in the 17th NIH research festival, a two-and-a-half-day event in October that highlighted intramural research. The festival, which began in 1986 and has been held annually since 1988, included four poster sessions on more than 20 topics, two minisymposia comprising 12 sessions, and a special job fair for postdoctoral and clinical fellows. This year, the festival was launched by major scientific symposia that celebrated the NIH Clinical Center's 50th anniversary.

DCEG poster presentations at the NIH Research Festival by Deirdre Hill, Lifang Hou, Wen-Yi Huang, Greg Kirk, Ruth Kleinerman, James Lacey, Qing Lan, Nickolas Luckyanov

Joseph F. Fraumeni, Jr., M.D., DCEG Director, was the 2003 festival cochair, along with Dr. Robert Desimone, Scientific Director of the National Institute of Mental Health. New additions to the research festival included a special poster section that focused on epidemiology. This subject area proved very successful; 72 posters were presented during the epidemiology section alone, making it the festival's largest poster session. More than 80 percent of the epidemiology posters described DCEG research projects.


NIH Director Elias Zerhouni with Joseph F. Fraumeni, Jr., at the NIH Research Festival

"The poster session indicated the enormous breadth of cutting-edge biomedical research taking place at NIH," Dr. Fraumeni said. "This provided a unique forum for NIH investigators to communicate with one another and to identify opportunities for collaborative interdisciplinary research."

The festival also featured a molecular epidemiology minisymposium cochaired by **Nathaniel Rothman, M.D., M.P.H., M.H.S.**, from the Occupational and Environmental Epidemiology Branch, and **Stephen Chanock, M.D.**, Director of the NCI Core Genotyping Facility. The session, titled "Using New 'Omics' in the Molecular Epidemiology of Chronic Diseases: Emergence of a New Paradigm," explored the clinical applications of proteomics, the use of gene expression profiling to identify cancer targets for diagnosis and treatment, the application of genetic variation in the study of cancer etiology, and the challenge of false-positive findings with these new genetic technologies. **Sholom Wacholder, Ph.D.**, of the Biostatistics Branch, gave the last presentation. ■