Division of Cancer Epidemiology and Genetics

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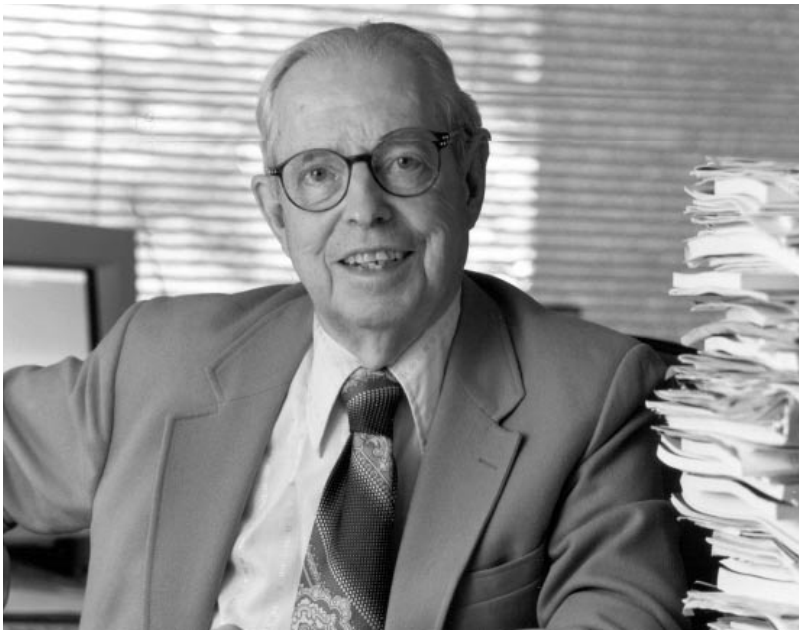
THE EXTRAORDINARY CAREER OF GILBERT BEEBE

Gilbert Wheeler Beebe, Ph.D., one of the world's leading authorities on radiation effects, recently retired at age 89 after a spectacular 60-year research career. Although "officially" retired, he plans to remain at NCI as Scientist Emeritus.



Dr. Gilbert Beebe

Born in Mahwah, New Jersey, in 1912, Dr. Beebe received a B.A. in sociology from Dartmouth College in New Hampshire and an M.A. (in sociology) and a Ph.D. (in sociology and statistics) from Columbia University in New York. He has worked for the National Committee on Maternal Health, the Milbank Memorial Fund, the U.S. Army's Office of the Surgeon General, the Hoover Commission (charged with reorganizing the executive branch of the government), the Atomic Bomb Casualty Commission, the National Research Council of the National Academy of Sciences, and—since 1977—NCI.

He has been author, co-author, or co-editor of five books and has published more than 130 journal articles and book chapters since 1936. Dr. Beebe has received the PHS Special Recognition Award and the NIH Director's Award in recognition of his work.

Dr. Beebe's involvement in radiation effects started after World War II, when he organized the Medical Follow-up Agency of the National Research Council to study the health effects of U.S. veterans' special exposures, conditions, and experiences during military service. His responsibilities extended to designing follow-up studies of Japanese citizens who survived the atomic bombs dropped on Hiroshima and Nagasaki. His extraordinary work as the architect of this pioneering research project laid the foundation for much of our current understanding of the carcinogenic effects of ionizing radiation. In 1977 Dr. Beebe joined NCI as a health statistician in the epidemiology program, and in 1994 he joined the Radiation Epidemiology Branch. When the Chornobyl Research Unit was formed within this Branch in 1999, he was appointed as its head.

Dr. Beebe's work at NCI has focused on the development of a highly complex and multidisciplinary project to study the health consequences of the 1986 accident at the Chornobyl nuclear facility in Ukraine. Dr. Beebe and staff members, in collaboration with investigators in Ukraine

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and Belarus and at Columbia University, are studying two groups:

- 73,000 children exposed to radioiodines, who are screened bienially for thyroid cancer. Risk analyses compare the carcinogenic effects of radioiodine with those of x-rays and gamma rays.

- 88,000 cleanup workers exposed to whole-body gamma radiation, who are followed to collect information on the risk of leukemia. The study should help clarify the risk of leukemia from radiation exposure and provide better estimates of the time lapse between exposure and development of the cancer.

The professional accomplishments of Dr. Beebe are many and varied, but his personality never belies the fact that he is generally considered the leading expert on radiation epidemiology. Colleagues remember his sense of humor—which he never hesitates to use on himself—and his underlying respect for others. They also mention tenacity, thoroughness, and "going the step beyond where others are satisfied or just tired."

"He is a very unselfish person who works hard, accomplishes much, writes well, speaks his mind clearly, and is articulate and careful to acknowledge those to whom credit is due," wrote Dr. A. Bertrand (Randy) Brill, a research professor at Vanderbilt University. "When asked for his comments he has always spoken out with a directness that I have found refreshing, even when it is something I did not want to hear."

Dr. Elena Buglova, from the Research Clinical Institute of Radiation Medicine and Endocrinology in Belarus, has worked closely with Dr. Beebe on the Chornobyl project. She called him "the father and grandfather of the project, advisor and consultant, expert and supervisor." She recalled: "Meetings with Dr. Beebe were a practical school in epidemiology. But this school was more pleasant than the usual one because of the kind character of Gil and his sense of humor." The first time Dr. Beebe cracked a joke, Dr. Buglova thought she had misunderstood his English—she did not expect "such a famous specialist" to say something funny.

Dr. Scott Davis, now chair of the Department of Epidemiology at the University of Washington, Seattle, first met Dr. Beebe when Dr. Davis was a newly minted Ph.D. working at the Radiation Effects Research Foundation (RERF) in Hiroshima. Dr. Davis was asked to present at the annual meeting of the Science Council findings from a study he initiated on pancreatic cancer. "This was a big event at RERF, with many dignitaries and experts in attendance," recalled Dr. Davis in a recent letter to Dr. Beebe. "I was scared to death."

After the presentation, Dr. Beebe asked to meet Dr. Davis and discuss the work. "You listened intently as I described my projects in more detail, you offered insightful advice and suggestions, and above all you were incredibly supportive and encouraging," remembered Dr. Davis. "Even though I was so clearly junior, you treated me like a colleague and with respect for my abilities and ideas. This made a huge impression on me at the time, motivated me to forge ahead at a critical juncture in my stay at RERF, and truly influenced my emerging interest in radiation studies."

Dr. Davis' closing words to Dr. Beebe capture the feelings of all who have worked with this eminent researcher: "You are greatly admired not only for your insightful scientific work and many contributions, but also for the kindness you show to others and the human touch that transcends all of your work." ■

—Nancy Volkers

DCEG RESPONSE TO TERRORISM

Following the September 11 attacks on the Pentagon and on the World Trade Center, DCEG members responded through service as members of special PHS teams and by strategically evaluating the staff and resources that could be mobilized in response to any future terrorist activities.

Captain Linda Morris Brown, Dr.P.H., of the Biostatistics Branch, and Lieutenant Junior Grade Claudine Samanic, M.S.P.H., of the Occupational Epidemiology Branch, were among the PHS Commissioned Corps Readiness Force (CCRF) officers deployed to assist in the relief effort. CAPT Brown helped contact members of the PHS-1 Disaster Medical Assistance Team when it was assigned to a 10-day mission caring for injured rescue workers in New York. She then served as a liaison between team members and their families during the mission.

LTJG Samanic went to New York as one of 30 CCRF members that supported the Disaster Mortuary Response Team, a federal-level response team that assists in cases of mass fatality. While there, she collected and entered reports of missing persons and processed medical and dental records. "One of the most difficult things to deal with was seeing the names, photographs, and personal information of all the victims," she said. "Processing packages containing hair samples and other items submitted for DNA recovery made us think of those who took the time to pack and send such items, and what they must have been feeling."

CAPT Brown and LTJG Samanic had just completed these tours when the first exposures to anthrax-contaminated mail were reported. As part of CCRF's response, LTJG Samanic was deployed again, this time to work with DHHS Secretary Tommy Thompson's Bioterrorism Emergency Command Center. CAPT Brown also was deployed, serving two tours as DHHS liaison to the Office of Homeland Security Emergency Support Team. In this role, she gathered information from DHHS on anthrax and other homeland health issues. The team, coordinated by the Federal Emergency Management Agency, used this information to brief former Pennsylvania Governor Tom Ridge, Director of the Office of Homeland Security.

CAPT Linda Brown and LTJG Claudine Samanic

Meanwhile, DCEG assessed its ability to respond to biological, chemical, or nuclear attacks, both at NIH and in general. At the request of DCEG Director Joseph F. Fraumeni, Jr., M.D., a working group headed by Neil Caporaso, M.D., of the Genetic Epidemiology Branch, examined the Division's resources and expertise. The working group made eight recommendations:

- **Identify skills that DCEG can use during an emergency.**
- **Provide training to upgrade skills.** Provide seminars on biological, chemical, and radiation exposures and offer a course conducted by former CDC Epidemic Intelligence Service Officers currently serving in DCEG.
- **Collaborate or advise on studies to understand the health consequences of terrorist actions.** Investigate occupational and environmental hazards faced by rescue workers and residents around the "ground zero" sites in New York and at the Pentagon, as well as studies in international locations. Use existing cohorts to assess

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baseline and changes in populations at high risk for exposure to bioterrorism, and identify new cohorts.

- **Contribute expertise to a rapid-response team of federal scientists prepared to tackle fast-breaking developments.**
- **Support efforts to expand health surveillance systems.**
- **Promote the development and application of technologies to detect infectious agents.** Technologies include those that enable rapid recognition of specific DNA sequences.
- **Protect critical infrastructures.** Update security and disaster plans for specimen repositories supported by DCEG, as well as repositories nationwide, and coordinate procedures with emergency response officials.
- **Enhance DCEG response to nuclear threats.** Help provide training for scientists at the Radiation Emergency Assistance Center/Training Site in Oak Ridge, Tennessee, and collaborate with the Armed Forces Radiobiology and Research Institute. Contribute to the development of an NIH response team, and help manage the medical needs of persons exposed to radiation and the use of personnel decontamination facilities.

Steven Simon, Ph.D., of the Radiation Epidemiology Branch, also prepared a report on possible terrorist activities involving radiation. The report described sources of radioactive materials, types of possible nuclear terrorism, and ways in which DCEG could respond. Dr. Simon cautioned that atomic bombs do not constitute the only means of nuclear terrorism; a conventional explosion such as a plane crash or car bomb could mask the dispersion of radiation. He therefore recommended that specialized instruments and personnel trained to look for radiation be available at potential disaster sites.

The researchers at DCEG, with their expertise in public health, molecular epidemiology, infectious diseases, chemical and radiation exposures, and statistics, represent a valuable resource in combating bioterrorism. Although the Division would most likely be involved in long-term assessment of the effects of a bioterrorist attack, many in DCEG, in addition to CAPT Brown and LTJG Samanic, can be called on to respond rapidly to a crisis. DCEG is creating a database of staff with specialized areas of expertise who could assist in an emergency. ■

—Frances McFarland, Ph.D.

DCEG DIVISION AND PROGRAM DIRECTORS RECEIVE NOTABLE AWARDS

Two pillars of the DCEG community recently received prestigious awards in recognition of their contributions to the fields of cancer epidemiology and public health.

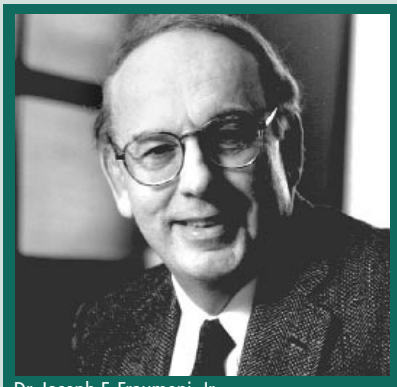
2002 Dr. Nathan Davis Award

The American Medical Association (AMA) awarded **Joseph F. Fraumeni, Jr., M.D.,** Director of DCEG, the 2002 Dr. Nathan Davis Award in the category of Member of the Executive Branch in Career Public Service. The awards, established in 1989 to honor the memory of Dr. Davis, AMA founder, recognize local, state, and federal government officials for outstanding public service in the advancement of public health. The AMA presents them on the recommendation of an independent panel of judges. Recipients of these awards are recognized as outstanding leaders in their field who have promoted the art and science of medicine and who have contributed greatly to the public health through elected or career government service.

2001 John Snow Award

The American Public Health Association (APHA) honored **Robert N. Hoover, M.D., Sc.D.,** Director of DCEG's Epidemiology and Biostatistics Program, with the John Snow Award at its annual meeting in Atlanta this past October. The award recognizes an outstanding epidemiologist who has made contributions of enduring value to the improvement of human health. It is named after Dr. John Snow (1813–1858), a legendary figure in the history of public health, who was the first to link the spread of an 1854 outbreak of cholera in central London to the use of a sewage-contaminated water pump. In accepting the award, Dr. Hoover said, "The name of the award, and its bestowal by the Epidemiology Section of the APHA, would be honor enough. The fact that my name will be added to a list of prior winners that includes the giants of our profession, whom I have revered and held in personal awe for my entire career, makes this a truly humbling experience."

—Katrina Wahl and Catherine McClave, M.S.



Dr. Joseph F. Fraumeni, Jr.

Dr. Robert N. Hoover

STEPHEN CHANOCK HEADS THE CORE GENOTYPING FACILITY

In September, Stephen Chanock, M.D., was named the Acting Director of the NCI Core Genotyping Facility (CGF) located at the Advanced Technology Center. Dr. Chanock received his medical degree from Harvard Medical School in 1983 and completed training in pediatrics, infectious diseases, and pediatric hematology/oncology at Boston Children's Hospital and the Dana-Farber Cancer Institute. He joined NCI in 1991, where he has been investigating the molecular, cellular, and clinical problems of infectious complications in patients with cancer and HIV infection. He also holds a dual appointment as a senior investigator in the Pediatric Oncology Branch of NCI's Center for Cancer Research. *DCEG Linkage* met with Dr. Chanock to discuss his plans for the future of the facility.

What is the function of the CGF?

The laboratory serves three major functions. The first is to develop and sustain a high-throughput genotyping facility to conduct current and planned studies. The second is to evaluate new technologies and approaches that could increase efficiency and throughput while decreasing cost, while at the same time compare technical platforms for genotype analysis, including single-base extension, chip-based amplification, and real-time amplification. Third, the facility will use sequence analysis to discover and validate common and, perhaps, rare variants: genetic analyses will be conducted on studies planned and executed by DCEG investigators to address fundamental questions in the prevention and treatment of cancer.

What are your plans for the laboratory?

The laboratory is undergoing reorganization, which includes hiring technical staff and bioinformatics support. To meet our goals, we need to train staff to use the three technical platforms available in the CGF for genotype analysis and to develop a flowthrough that will analyze genotypes on more than one technical platform. Because a large number of genotypes are needed to address DCEG requests, we are concentrating on substantially increasing the number of available genotypes in coordination with NCI's so-called "SNP 500," which now exceeds 650 single-nucleotide polymorphisms (SNPs) that have been resequenced in a reference set of 102 samples.

The long-term, and for that matter, short-term effects of developing algorithms for correlating disease outcomes with genetic variation have implications for not only medical care, but also the way in which care is to be delivered and the way in which the public will decide many important political and social questions.

We also intend to have project managers who will oversee the execution of work and be a clear reference point for communicating with principal investigators. We are hiring several persons with skill in applying current bioinformatic tools for genomic or genotype analysis. We plan to have "office hours" in Executive Plaza South, during which DCEG investigators can learn how to use the tools at the same time they search for suitable candidate genotypes for analysis. This added service should facilitate collaborations and the generation of data sets relevant to identifying functionally important SNPs.

Dr. Stephen Chanock

What tangible benefits do you think we will see over the next few years as a result of the genetics work being done in DCEG?

The long-term, and for that matter, short-term effects of developing algorithms for correlating disease outcomes with genetic variation have implications for not only medical care, but also the way in which care is to be delivered and the way in which the public will decide many important political and social questions. It would be naive to predict exactly how and what will change, but certainly the ability to tailor medicine based on individual profiles is promising. The irony is that the information

will have to be derived from population-based studies, ones that permit comparisons of sets of genetic markers. To be more specific, we are going to have to look toward larger studies than ever before, something that NCI clearly has set as a major priority. The tangible benefits derived from DCEG studies will be based on sound epidemiologic and laboratory data and these benefits will also include our ability to advance analytical techniques in genotyping. I fully expect that the advances will affect how cancer prevention and treatment are practiced in the years to come, but I can't predict the exact outcomes.

How will your training and experiences in infectious diseases and in pediatric hematology/oncology help you with your new mission?

Of course, these experiences influence my work substantially and reflect my training in clinical medicine. The world of clinical infectious diseases is, in part, the practical application of "running the numbers" on a disease, including the incidence and treatment effects from antibiotics. One has to also consider the host side—in other words, immune function. A background in infectious diseases has provided me with a working knowledge of epidemiology. This background should be especially useful in investigating cancers of the immune system, such as leukemias and lymphomas. Moreover, many experts have recently emphasized the importance of inflammation in the pathogenesis of certain cancers. How the host responds to infection can be modulated by common variants in critical genes of the immune pathways. Some of the same variants appear to influence the risk for acute and chronic infections. Understanding the general molecular principles behind diseases crosses over into many fields. While the specific genes, genetic pathways, or genetic alterations involved may be different for different diseases, some underlying principles are similar.

The tangible benefits derived from DCEG studies will be based on sound epidemiologic and laboratory data and these benefits will also include our ability to advance analytical techniques in genotyping.

From a clinical aspect, my experiences treating children with cancer not only taught me to think about the disease processes inherent to understanding cancer, but also put into perspective my personal and professional life. The world of pediatric oncology relies on a close interaction between family, patient, and medical team—one that is predicated on honest and, at times, frank and brutal discussions. The lessons learned can't be forgotten and, in fact, remind us to be direct and decisive in making decisions. I can't help but think that having treated individual children with cancer or other devastating diseases necessitates a degree of humility and, at the same time, a resolve to do something about it.

So while the clinical perspective helps me have a better understanding of the applicability of what we are doing here in the CGF, the personal experiences of being a pediatric oncologist keep me motivated to figure out what causes cancer.

You have had a role in running special programs for children with cancer. Has this role influenced your work?

Every summer I run the medical team for Camp Fantastic, an NCI-supported week of camp for children 7 to 17 years old who are on active therapy or off therapy for less than three years. We take about 100 children and a full medical staff and provide these kids with the opportunity to enjoy a camp setting despite the limitations mandated by treatment. It resets my internal compass and reminds me why I do what I do and the urgency with which it must be approached. I couldn't imagine missing this opportunity. In fact, I set my calendar by this week. During this time, one can't help but be drawn into the world of the children, many of whom face difficult circumstances. In a personal manner, it is humbling to be among so many special children. ■

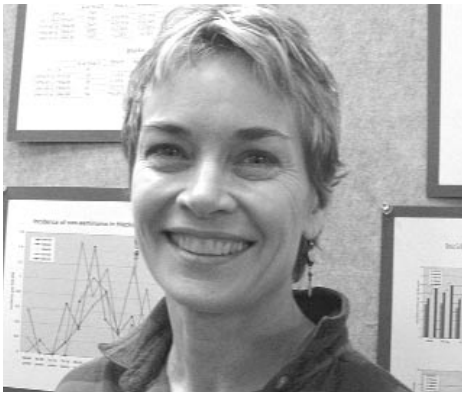
—Sandy Rothschild

TESTICULAR CANCER STUDY: DCEG LAUNCHES COLLABORATION WITH DEPARTMENT OF DEFENSE

Testicular tumors are the most common type of cancer among U.S. men aged 15 to 34 years. Because the military is largely composed of men in this age range, testicular cancer is the most frequently occurring cancer among this population. Known risk factors include prior history of testicular cancer, the failure of one or both testes to descend into the scrotum, and a family history of testicular cancer. The risk attributable to these factors, however, is only between 10 and 15 percent; thus, the majority of testicular cancer remains unexplained. Early age of onset and its association with undescended testis suggest, however, that the tumor may originate *in utero*.

Investigators in DCEG and the Department of Defense (DoD) are collaborating on a study of testicular germ cell tumors among U.S. military servicemen. This study will be the first large epidemiologic study to examine whether prediagnostic gonadotropin levels or endocrine modulators affect the risk of developing the tumor. In addition to having the optimal study population for testicular cancer, the DoD has an extremely valuable resource for case-control studies—the DoD Serum Repository. Begun in 1988 by the U.S. Army to store excess sera from HIV screening, the Repository now contains approximately 20 million serum samples from members of all service branches. The ability to link the Repository database with military medical records provides the possibility of examining many etiologic hypotheses for a wide variety of cancers and other diseases.

Researchers are identifying the case and control subjects for the study from among all men who have contributed samples to the DoD Serum Repository, and they are examining the serum samples for levels of organochlorines, gonadotropins, and viruses. The researchers are also asking the men's mothers to enroll in the study to provide invaluable information in determining the relationship between maternal exposures or events and testicular cancers in sons. All case subjects, control subjects, and mothers will donate a buccal cell sample and complete an interviewer-administered questionnaire. Researchers launched the study in February 2002 and anticipate the interview phase of the study will continue through mid-2003. Katherine McGlynn, Ph.D., of the Environmental Epidemiology Branch



Dr. Katherine McGlynn

is leading the study, along with DCEG co-investigators Barry Graubard, Ph.D., Louise Brinton, Ph.D., Robert Hoover, M.D., and James Goedert, M.D. ■

—Katherine McGlynn, Ph.D.

NEW REPRESENTATIVES TO NIH FELLOWS COMMITTEE

In October, Sowmya Rao, Ph.D., of the Biostatistics Branch, and Sam Mbulaiteye, M.D., of the Viral Epidemiology Branch, began serving on the NIH Fellows Committee (FELCOM). Before becoming an official member of FELCOM, Dr. Rao collaborated with Sholom Wacholder, Ph.D., of the Biostatistics Branch on the statistical analysis of an NIH Fellows Survey. By joining the postdoctoral committee, Dr. Rao hopes "to ensure that our fellows' experience meets or even exceeds their expectations." Dr. Mbulaiteye, whose profile was featured in the last issue of *DCEG Linkage,* aims "to bridge the gap between awareness and participation in FELCOM activities" during his service on the committee.

Drs. Sowmya Rao and Sam Mbulaiteye

FELCOM (*http://www.felcom.nih.gov/*) serves more than 3,000 fellows in training at NIH by sponsoring activities such as career development training and the Fellows Award for Research Excellence (FARE) travel competition, and by serving as a voice on important fellowship issues to the NIH leadership.

We thank Tatiana Dracheva, Ph.D., of the Laboratory of Population Genetics and Dawn Elizabeth McNeil, M.D., of the Genetic Epidemiology Branch for serving as DCEG representatives to FELCOM this past year.

—Kris Kiser, M.H.A.

NIH ACADEMY FELLOW VANESSA SHAW

DCEG is pleased to welcome its first NIH Academy Fellow, Vanessa Shaw. A determined, hardworking student with academic and research training, Ms. Shaw graduated in May 2000 from Hampton University in Virginia with a degree in biology. She entered the NIH Academy fellowship in September 2000, initially in an NCI developmental biology laboratory, then joined DCEG beginning in September 2001.

Ms. Shaw is working primarily with Dr. Michael Alavanja, of the Occupational Epidemiology Branch, on the Agricultural Health Study examining the health implications of economic disparities between large and small farms. She is also exploring the possibility of working with Dr. Susan Devesa, of the Biostatistics Branch, to examine risk factors for prostate cancer and their relationship to the geographic distribution of mortality from this cancer. Finally, Dr. Linda Morris Brown, also of the Biostatistics Branch, will guide Ms. Shaw in a project exploring the causes for the higher rate of esophageal cancer among African Americans than among whites, by investigating racial differences with respect to genetic and molecular markers of susceptibility and their interaction with environmental and lifestyle factors.

"My number one goal for my fellowship in DCEG is to gain experience in epidemiology prior to entering a graduate program in public health in the fall of 2002," said Ms. Shaw. "By working on a project that requires me to know and use biostatistics, taking an introductory epidemiology course, and attending the DCEG seminars, I hope to be well prepared for graduate study."

This past summer, while completing her work in the NCI laboratory, Ms. Shaw attended the NCI Summer Curriculum in Cancer Prevention, offered through

Ms. Vanessa Shaw

the Division of Cancer Prevention. This past fall, she enrolled in the Foundation for Advanced Education in the Sciences course Introduction to Epidemiology, and she is learning biostatistics and SPSS. During her first months at DCEG, Ms. Shaw met daily with Dr. Alavanja for the hands-on guidance needed to launch her epidemiology research projects. Dr. Alavanja described being a mentor for a postbaccalaureate fellow as "an important and rewarding experience because of the potential positive influence you have on a young person's professional development. A humbling experience with the realization that you really do have an influence. A hopeful experience—that is, giving your best will have a net positive effect. In practice, it's simply fun, since Vanessa is such a sweet, hardworking, and bright person!"

The NIH Academy Fellowship provides opportunities for recent college graduates to spend a year in biomedical research at NIH. Through these opportunities, the Academy aims to enhance research dedicated to the elimination of domestic health disparities through the development of a diverse cadre of biomedical researchers. For more information about the program, visit *http://www.training.nih.gov.* ■

—Kris Kiser, M.H.A.

Ms. June Peters

CLINICAL GENETICS BRANCH APPROVED AS CERTIFIED GENETIC COUNSELING SITE

This fall, the American Board of Genetic Counselors (ABGC) certified DCEG's Clinical Genetics Branch (CGB) as an approved training site for the joint NIH–Johns Hopkins University genetic counselor training program. Most genetic counselors hold a master's degree from ABGC-accredited programs and become board certified after passing the ABGC national certification examination. The CGB certification effort was led by genetic counselor June Peters, M.S., who is also in the process of obtaining training accreditation with genetic counseling programs at Howard University and the University of Maryland.

Under the current program, students spend a two-month rotation in CGB gaining exposure to genetic counseling in the clinical research setting. Under the joint tutelage of Ms. Peters and Ann Carr, M.S., a genetic counselor with Westat, students encounter an array of medical, genetic, and psychosocial issues faced by individuals and families dealing with hereditary cancers. The first CGB intern, Elizabeth Lardy, arrived for her rotation in November. Ms. Peters said, "We are thrilled to be working with our first student from the NIH–Johns Hopkins University program, since their training is unique in the combination of clinical genetics, counseling, and research skills that the students acquire."

—Kris Kiser, M.H.A.

FEASIBILITY STUDIES FOR RESEARCH ON FARMWORKERS

The November 2001 issue of the *American Journal of Industrial Medicine* was a special volume of 15 papers on a series of pilot projects designed to assess the feasibility of conducting epidemiologic research on migrant and seasonal farmworkers. **Shelia Zahm, Sc.D.,** DCEG's Deputy Director, and **Aaron Blair, Ph.D.,** of the Occupational Epidemiology Branch (OEB), served as guest editors. Together, they led a team of researchers and migrant healthcare workers from approximately 20 institutions on projects that addressed designing questionnaires, ascertaining pesticide exposures, tracing, evaluating cancer incidence and mortality, and establishing a cohort of farmworkers for future follow-up.

Using an approach first designed at the University of Washington, this team developed a questionnaire to ascertain detailed occupational histories via a life events/icon calendar. The questionnaire, which also collected information on numerous cancer risk factors, was pretested in nine locations across the United States. OEB's **Larry Engel, Ph.D.,** evaluated the questionnaire's reliability over time and its performance relative to a traditional method of collecting work histories. **Joanne Colt, M.S., M.P.H.,** also of the OEB, assessed the comparability of work histories obtained from the farmworkers with proxy reports from their spouses. She also studied mortality patterns among farmworkers on the basis of death certificate data from 24 states. OEB members **Mary H. Ward, Ph.D.,** and **Patricia Stewart, Ph.D.,** reported on projects to impute the probability of pesticide exposure from the occupational histories. Other projects involved the correlation of biological measures of pesticide exposure to questionnaire data on work practices, comparisons of pesticide metabolites in maternal urine and cord blood, locating farmworkers 10 years after first contact, and a study of cancer incidence among members of the United Farmworkers of America. It is hoped that this work will stimulate and encourage other investigators to conduct research on farmworkers that will uncover clues to cancer etiology and lead to improvements in the health of this underserved population. ■

—Shelia Zahm, Sc.D.

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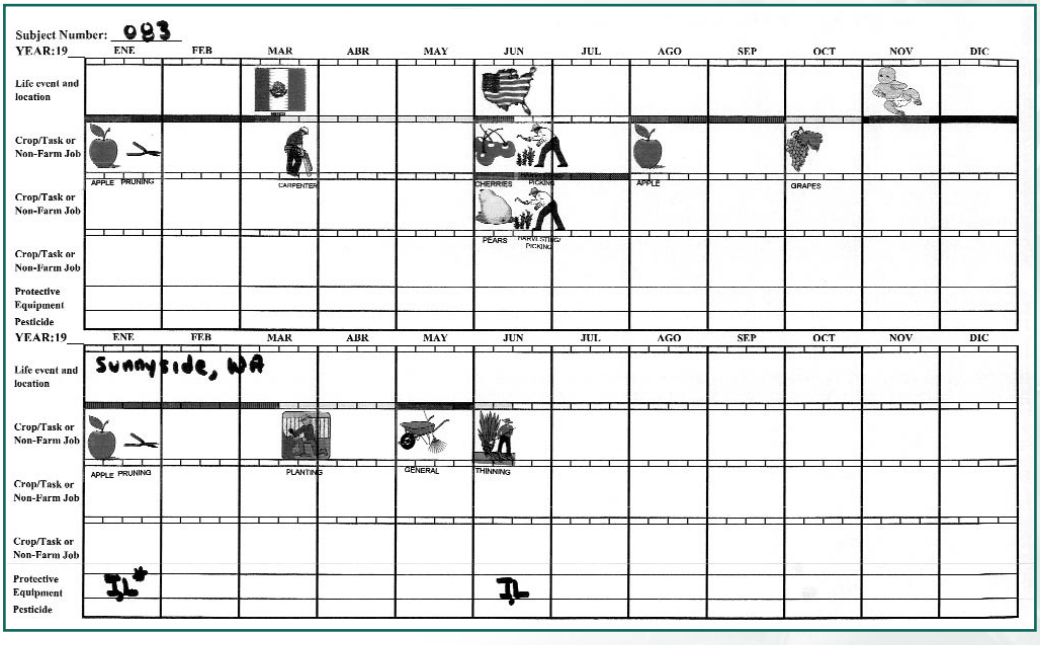


Life events/icon calendar

NEW QUESTIONNAIRE MODULE WEB SITE

Recently, DCEG launched a new public web site, QMOD, which contains questionnaire modules available for use in epidemiologic studies. QMOD, created by B.J. Stone, Ph.D., of the Biostatistics Branch, was brought to fruition with the help of Laure El ghormli, M.S., also of the Biostatistics Branch, and Roberta McClimens of Information Management Systems, Inc. The site can be found at *http://dceg.cancer.gov/QMOD/*.

Intended as a tool for researchers trying to develop questionnaires, QMOD consists of a collection of 69 questionnaire modules and a search mechanism for finding modules that correspond to a given topic, investigator, or study title. There is also a list of references that could be helpful to the researcher in creating a questionnaire, as well as links to useful model questionnaires.

Most of the modules in the collection come from questionnaires designed and used by DCEG researchers. These questionnaires have produced data that have been analyzed by DCEG researchers. The modules, selected for their clarity, sensitivity of language, and completeness, are usually accompanied by citations to articles describing the analysis results. It is hoped that other researchers can adapt the modules to their particular needs.

QMOD has been used successfully by DCEG researchers for some time. With the new web site, scientists from other organizations can take advantage of these tools as well. ■

—B.J. Stone, Ph.D.

Dr. B.J. Stone, Ms. Roberta McClimens, and Ms. Laure El ghormli

Drs. Edward Trapido, Audrey Saftlas, and Lynn Levin

Drs. Janet Stanford and Larry Figg

Drs. Paul Levine, Rolando Herrero, and Alex Kramer

DCEG ALUMNI REUNION 2001

For the past 40 years, NCI has had an active, growing, world-class intramural research program in cancer epidemiology. Since its inception in 1961 with the arrival of Robert W. Miller, M.D., Dr.P.H., now Scientist Emeritus, the program has grown to eight branches and a staff of more than 200 and is now the DCEG. The Division has played a vital role in developing the field of cancer epidemiology and related areas. To celebrate four decades of epidemiologic research excellence, a DCEG Alumni Meeting was held during the June 2001 Congress of Epidemiology in Toronto. Over 400 former DCEG researchers (postdoctoral fellows, principal investigators, and visiting scientists) throughout the world were invited to the event, representing a vast array of careers, expertise, and institutions.

The evening was a grand success. Highlights included warm and collegial reminiscences and an impressive photographic display of DCEG researchers throughout the decades, in both serious and not-so-serious settings and attire. The photos had been provided by Division staff and assembled by Samantha Nhan, of DCEG's Office of the Director. They revived many fond memories and illustrated the amazing changes that have taken place at NCI over the years. The considerable effort that went into gathering alumni addresses and data on professional interests will also provide a rich recruitment tool to advertise our fellowship programs and assist career placement for our pre- and postdoctoral fellows.

—Kris Kiser, M.H.A.

NCI–CHINA COLLABORATIVE BILIARY TRACT CANCER STUDY

Biliary tract cancer, which encompasses cancers of the gallbladder, extrahepatic bile duct, and ampulla of Vater, is a rare cancer. Other than gallstones, the etiology of biliary tract cancer is poorly understood. In Shanghai, China, the incidence of biliary tract cancer is rising more rapidly than the incidence of any other malignancy. As in other countries, gallbladder cancer is the most common subsite and occurs more often among women than men. To further elucidate the etiology of biliary tract cancer and reasons for the rapid increase in incidence, Ann Hsing, Ph.D., of the Environmental Epidemiology Branch, joined forces with the Shanghai Cancer Institute and launched a collaborative study of biliary tract cancer in 1997.

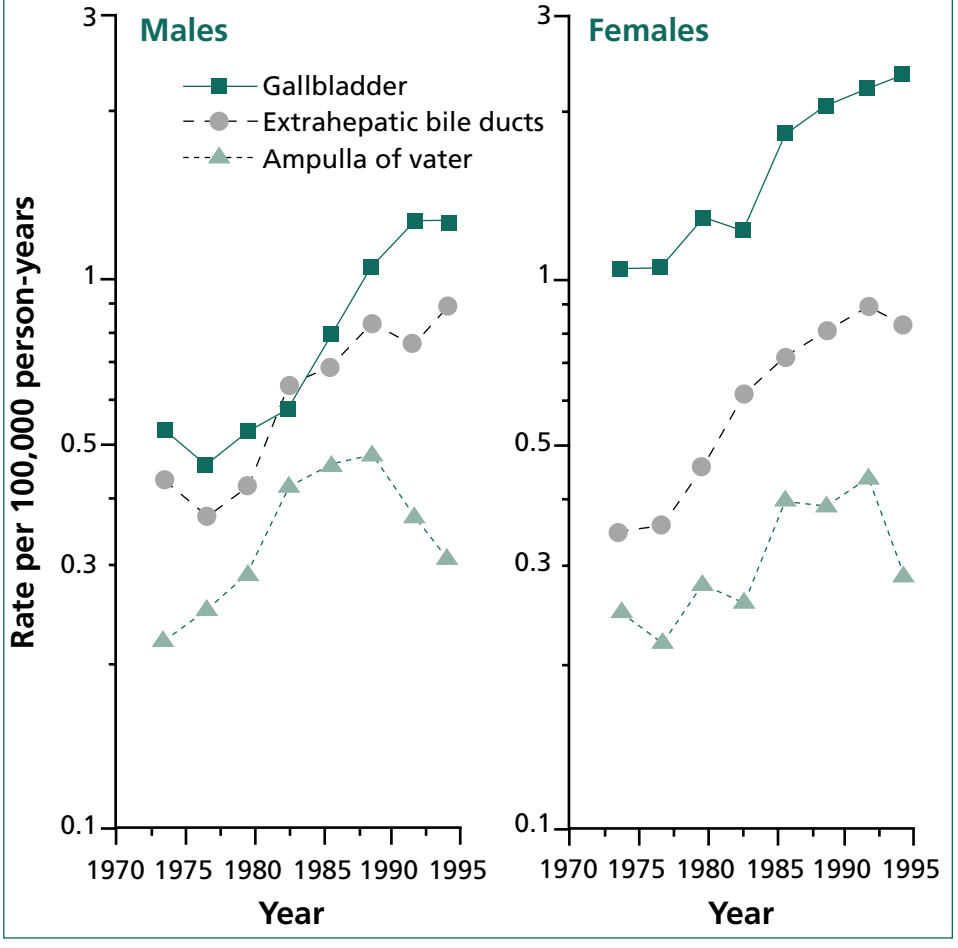
This complex, multidisciplinary, population-based case-control study is the largest and most comprehensive ever for biliary tract cancer. The study enrolled nearly 3,000 persons, including 891 case subjects with cancer (485 gallbladder, 278 bile duct, and 128 ampulla of Vater), 1,035 control subjects with gallstones, and 1,005 healthy subjects randomly selected from the population. Case ascertainment rate and response rates for interviews were more than 95 percent. The study has an extensive biochemical and molecular component, with more than 85 percent of the subjects providing 20 mL of fasting blood and 24-hour urine samples, along with the collection of bile samples, gallstones, and fresh and fixed tissue samples from patients undergoing surgical resection of the biliary tract.

Data collection was successfully completed in July 2001. More than 45,000 vials of biological specimens, including 26,000 vials of DNA samples, have been stored at the NCI repository in Frederick. Collaboration with the Shanghai Cancer Institute, M.D. Anderson Cancer Center, Johns Hopkins University, Massachusetts Institute of Technology, and Wake Forest Genome Center is actively under way to evaluate several key etiologic hypotheses (including *Helicobacter* species in bile samples, chronic infection with hepatitis B virus, serum levels of various lipid fractions, and bile acid and cholesterol contents in gallstones) as well as genetic susceptibility related to lipid and hormone metabolism. Researchers are performing genome-wide allelotyping of tumor tissue to investigate loss of heterozygosity in tumor suppressor genes that may be involved in the genesis of biliary tumors.

The NCI–China Collaborative Biliary Tract Cancer Study provides a unique opportunity to uncover the etiology of biliary tract cancer. The extensive collection of epidemiologic and clinical data along with biological specimens represents a rich resource to test emerging etiologic hypotheses with state-of-the-art techniques. ■

—Ann Hsing, Ph.D.

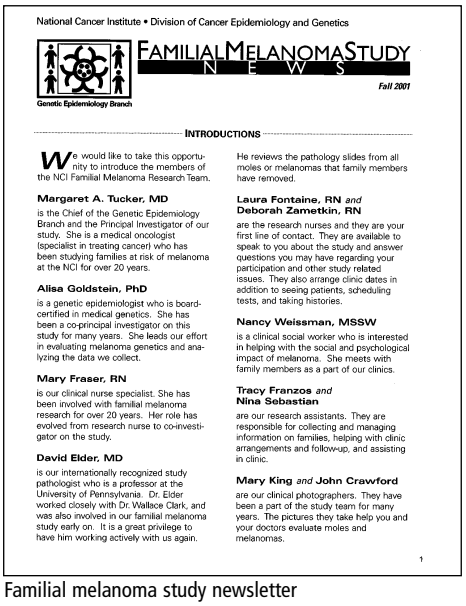
Age-adjusted incidence trends for biliary tract cancers in urban Shanghai by subsite, sex, and year of diagnosis, 1972–74 to 1993–94



FAMILIAL MELANOMA STUDY NEWSLETTER

The Genetic Epidemiology Branch has published a newsletter, *Familial Melanoma Study News,* for families enrolled in the NCI Familial Melanoma Study. Margaret Tucker, M.D., Branch Chief, Alisa Goldstein, Ph.D., Chief of the Population and Statistical Genetics Section, and Mary Fraser, R.N., M.A., Clinical Nurse Specialist, developed the content of the newsletter, which was mailed to approximately 2,000 family members, some of whom have been participating in the study since its inception in 1976. In addition to updating study participants on the staff currently involved in the project, the newsletter contains a brief memorial for Dr. Wallace Clark, Jr., who died in 1997. Dr. Clark, a world-renowned dermatopathologist and clinician, was instrumental in launching this study, defining the clinical and histologic features of dysplastic nevi and their evolution to melanoma, and significantly advancing knowledge about the management of familial melanoma.

Other articles in the newsletter discuss the continued increasing incidence of melanoma in the general population, particularly in men over 50 years of age



National Cancer Institute • Division of Cancer Epidemiology and Genetics

FAMILIAL MELANOMA STUDY NEWS

Fall 2001

Genetic Epidemiology Branch

INTRODUCTIONS

We would like to take this opportunity to introduce the members of the NCI Familial Melanoma Research Team.

Margaret A. Tucker, MD is the Chief of the Genetic Epidemiology Branch and the Principal Investigator of our study. She is a medical oncologist (specialist in treating cancer) who has been studying families at risk of melanoma at the NCI for over 20 years.

Alisa Goldstein, PhD is a genetic epidemiologist who is board-certified in medical genetics. She has been a co-principal investigator on this study for many years. She leads our effort in evaluating melanoma genetics and analyzing the data we collect.

Mary Fraser, RN is our clinical nurse specialist. She has been involved with familial melanoma research for over 20 years. Her role has evolved from research nurse to co-investigator on the study.

David Elder, MD is our internationally recognized study pathologist who is a professor at the University of Pennsylvania. Dr. Elder worked closely with Dr. Wallace Clark, and was also involved in our familial melanoma study early on. It is a great privilege to have him working actively with us again. He reviews the pathology slides from all moles or melanomas that family members have removed.

Laura Fontaine, RN *and* **Deborah Zametkin, RN** are the research nurses and they are your first line of contact. They are available to speak to you about the study and answer questions you may have regarding your participation and other study related issues. They also arrange clinic dates in addition to seeing patients, scheduling tests, and taking histories.

Nancy Weissman, MSSW is a clinical social worker who is interested in helping with the social and psychological impact of melanoma. She meets with family members as a part of our clinics.

Tracy Franzos *and* **Nina Sebastian** are our research assistants. They are responsible for collecting and managing information on families, helping with clinic arrangements and follow-up, and assisting in clinic.

Mary King *and* **John Crawford** are our clinical photographers. They have been a part of the study team for many years. The pictures they take help you and your doctors evaluate moles and melanomas.

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Familial melanoma study newsletter

and in women in their 20's and 30's; the recently updated skin care guidelines for the prevention and early detection of melanoma, including the need for all members of melanoma-prone families (not just those with dysplastic nevi or melanoma) to follow these guidelines; a brief summary of the genetics of melanoma, noting that although two melanoma susceptibility genes—*CDKN2A* and *CDK4*—have been identified, other genes and gene-environment factors likely play a role in the development of melanoma; information about the Melanoma Genetics Consortium; an update about the 1999 Food and Drug Administration sunscreen regulations, highlighting the sunscreen labeling issues; and a list of several relevant web sites along with a description of the information available. The web sites include NCI's cancer information page (*http://cancer.gov*), the Centers for Disease Control and Prevention's "Choose Your Cover" sun-safe education, the Environmental Protection Agency's "Sunwise" and ultraviolet index information sites, and the Food and Drug Administration's on-line consumer information article, "Trying to Look SUNsational? Complexity Persists in Using Sunscreens."

Newsletters such as this one are an excellent way to keep study participants informed about the progress of the research, which would not be possible without the generous and continued participation of these dedicated persons, and to review and reinforce those health behaviors recommended to decrease the burden of melanoma in their families. ■

—Mary Fraser, R.N., M.A., and Barbara Rogers

DNA REPAIR WORKSHOP

Dr. Richard Pelroy of NCI's Division of Cancer Biology and **Alice Sigurdson, Ph.D.,** of DCEG's Radiation Epidemiology Branch cochaired a workshop entitled "Radiation Sensitivity, Cancer Susceptibility, and Common DNA Repair Polymorphisms (SNPs)" held November 7–9, 2001. The workshop highlighted NCI's research efforts in DNA repair and generated interest and potential collaborations with university researchers.

Keynote presentations provided an overview of radiation epidemiology and the resources available to study gene-radiation interactions, issues of multiple comparisons, the most recent advances in structural biology and protein-protein interfaces, and the complexity of maintaining genomic integrity. Approximately 60 persons representing such disciplines as molecular biology, mouse models, and epidemiology attended from the United States and England. **Stephen Chanock, M.D.,** of the Core Genotyping Facility, **Elaine Ron, Ph.D.,** of the Radiation Epidemiology Branch, and **Sholom Wacholder, Ph.D.,** of the Biostatistics Branch were among the invited opening speakers.

Attendees learned of a growing body of molecular data that can help epidemiologists determine where informative single-nucleotide polymorphisms (SNPs) will likely occur in genes encoding DNA-repair proteins. Such SNPs could cause these proteins to function abnormally, hindering their ability to excise mutations that cause diseases. Studies in mice show that different genetic backgrounds can influence the effects of SNPs. **Jeffery Struewing, M.D.,** and **Kent Hunter, Ph.D.,** both of the Laboratory of Population Genetics, and Dr. Chanock drove home these points and highlighted resources such as NCI's "SNP 500."

Written summaries from the keynote speakers and session discussions, led by **Nathaniel Rothman, M.D., M.P.H., M.H.S.,** of the Occupational Epidemiology Branch, will be incorporated into a workshop proceedings for publication next year. Communication between the workshop participants will continue through a shared database, annual meetings, and other means.

—Alice Sigurdson, Ph.D.

RECENT SCIENTIFIC HIGHLIGHTS

CERVICAL CANCER

Cervical Inflammation and High-grade Cervical Neoplasia in Women Infected with Oncogenic Human Papillomavirus

A case-control study was conducted among women less than 50 years old enrolled in the Costa Rican natural history study of human papillomavirus (HPV) and cervical neoplasia. A marginally significant positive trend of increasing cervical inflammation was associated with high-grade lesions in oncogenic HPV-infected women (p for trend = 0.05). Overt cervicitis was associated with a 1.9-fold increase in risk of high-grade lesions (95 percent CI = 0.9–4.1). Cervical inflammation may be associated with high-grade lesions and may be an etiologic cofactor in women infected with oncogenic HPV. **(Castle PE, Hillier SL, Rabe LK, Hildesheim A, Herrero R, Bratti MC, Sherman ME, Burk RD, Rodriguez AC, Alfaro M, Hutchinson M, Morales J, Schiffman M. An association of cervical inflammation with high-grade cervical neoplasia in women infected with oncogenic human papillomavirus (HPV).** ***Cancer Epidemiol Biomarkers Prev*** **2001;10:1021-1027)**

Human Leukocyte Antigen Alleles and Risk of Cervical Neoplasia

To examine human leukocyte antigen (HLA) involvement in the development of all grades of cervical neoplasia, a nested case-control study of 10,077 women in Guanacaste, Costa Rica, was conducted. Compared with women who were negative for human papillomavirus (HPV), women with *HLA-DRB1*1301* had a significantly decreased risk for cancer or high-grade squamous intraepithelial lesions (odds ratio [OR] = 0.4) and for low-grade squamous intraepithelial lesions or HPV (OR = 0.6). Women with both *HLA-B*07* and *HLA-DQB1*0302* had an 8.2-fold increased risk for cancer or high-grade lesions (95 percent CI = 1.8–37.2) and a 5.3-fold increased risk for low-grade lesions or HPV (95 percent CI = 1.2–23.7). These results support the hypothesis that multiple risk alleles are needed to increase risk for cervical neoplasia, although a single allele may be sufficient for protection. **(Wang SS, Wheeler CM, Hildesheim A, Schiffman M, Herrero R, Bratti MC, Sherman ME, Alfaro M, Hutchinson ML, Morales J, Lorincz A, Burk RD, Carrington M, Erlich HA, Apple RJ. Human leukocyte antigen class I and II alleles and risk of cervical neoplasia: Results from a population-based study in Costa Rica.** ***J Infect Dis*** **2001;184:1310-1314)**

Folate and Invasive Cervical Cancer

The relationship between serum or red blood cell (RBC) folate and incident invasive cervical cancer was examined in a large, multicenter, community-based case-control study. For serum folate, the multivariate-adjusted odds ratio in the lowest versus highest quartile was 1.3 using the microbiologic assay and 1.6 using the radiobinding assay. For RBC folate, the comparable odds ratios were 1.2 and 1.5. Similar risks were obtained when analyses were restricted to subjects with a history of human papillomavirus infection. Thus, low serum folate and low RBC folate were moderately but nonsignificantly, associated with increased invasive cervical cancer risk. **(Weinstein SJ, Ziegler RG, Frongillo EA, Colman N, Sauberlich HE, Brinton LA, Hamman RF, Levine RS, Mallin K, Stolley PD, Bisogni CA. Low serum and red blood cell folate are moderately but nonsignificantly associated with increased risk of invasive cervical cancer in U.S. women.** ***J Nutr*** **2001;131:2040-2048)**

CHORDOMA

Familial Chordoma and Chromosome 7q33

A genome-wide analysis for linkage in a family with 10 individuals affected by chordoma, a tumor of notochordal remnants, yielded a maximum two-point LOD score of 2.21 at recombination fraction 0, at marker D7S2195 on chromosome 7q, based on the affected individuals only. Combined analysis of additional members of this family (11 affected individuals) and of two unrelated families (one with 2 affected individuals and one with 3 affected individuals), with 20 markers on chromosome 7q, showed a maximum two-point LOD score of 4.05 at marker D7S500. These results map a locus for familial chordoma to chromosome 7q33. **(Kelley MJ, Korczak JF, Sheridan E, Yang XH, Goldstein AM, Parry DM. Familial chordoma, a tumor of notochordal remnants, is linked to chromosome 7q33.** ***Am J Hum Genet*** **2001;69:454-460)**

COLORECTAL ADENOMAS

Mutagens from Meat-derived Heterocyclic Amines and Risk of Colorectal Adenomas

In a case-control study of colorectal adenomas, intake of the heterocyclic amines (HCAs) DiMeIQx, MeIQx, and PhIP and mutagenic activity were estimated through use of a meat-derived HCA and mutagen database and responses from a questionnaire module on meat cooking. The odds ratio for the fifth versus first quintiles was 2.2 for DiMeIQx (p for trend = 0.02), 2.1 for MeIQx (p for trend = 0.002), 2.5 for PhIP (p for trend = 0.02), and 3.1 for mutagenic activity (p for trend = 0.001). When each HCA was adjusted for the other two, only the trend for MeIQx (p = 0.04) remained statistically significant. Mutagenic activity from consumption of cooked meat, a measure that integrates all classes of mutagens, was strongly associated with risk and explained the excess risk with intake of well-done red meat. **(Sinha R, Kulldorff M, Chow WH, Denobile J, Rothman N. Dietary intake of heterocyclic amines, meat-derived mutagenic activity, and risk of colorectal adenomas.** ***Cancer Epidemiol Biomarkers Prev*** **2001;10:559-562)**

DIETHYLSTILBESTROL

Diethylstilbestrol and Incidence of Squamous Neoplasia of the Cervix and Vagina

Women exposed prenatally to diethylstilbestrol (DES) have an excess risk of clear cell adenocarcinoma of the vagina and cervix, but the effect of prenatal DES exposure on the incidence of squamous neoplasia is uncertain. A cohort of 3,899 exposed and 1,374 unexposed daughters was followed for 13 years (1982–1995) for pathology-confirmed diagnosis of high-grade squamous intraepithelial neoplasia of the genital tract. Based on 111 cases of high-grade disease, the relative risk among DES-exposed versus unexposed daughters was 2.1 (95 percent CI = 1.2–3.8). Risk estimates were higher with earlier intrauterine exposure: the relative risk for exposure within seven weeks of the mother's last menstrual period was 2.8 (95 percent CI = 1.4–5.5). **(Hatch EE, Herbst AL, Hoover RN, Noller KL, Adam E, Kaufman RH, Palmer JR, Titus-Ernstoff L, Hyer M, Hartge P, Robboy SJ. Incidence of squamous neoplasia of the cervix and vagina in women exposed prenatally to diethylstilbestrol (United States).** ***Cancer Causes Control*** **2001;12:837-845)**

Infertility among Women Exposed to Diethylstilbestrol Prenatally

A total of 1,753 women exposed to diethylstilbestrol (DES) prenatally and 1,050 unexposed women provided data on difficulties in conceiving and reasons for the difficulty. A greater proportion of exposed than unexposed women were nulligravid (relative risk [RR] = 1.3, 95 percent CI = 1.1–1.5), and a greater proportion had tried to become pregnant for at least 12 months without success (RR = 1.8, 95 percent CI = 1.6–2.1). DES exposure was significantly associated with infertility resulting from uterine problems (RR = 7.7, 95 percent CI = 2.3–25.0) or tubal problems (RR = 2.4, 95 percent CI = 1.2–4.6). **(Palmer JR, Hatch EE, Rao RS, Kaufman RH, Herbst AL, Noller KL, Titus-Ernstoff L, Hoover RN. Infertility among women exposed prenatally to diethylstilbestrol.** ***Am J Epidemiol*** **2001;154:316-321)**

ESOPHAGEAL AND GASTRIC CANCERS

Family History and Risk of Esophageal and Gastric Cancers

A multicenter, population-based, case-control study of 1,143 case subjects and 695 control subjects showed that persons reporting a family history of digestive cancers experienced no increased risk of either type of esophageal cancer (adenocarcinoma or squamous cell cancer), but they were prone to adenocarcinomas of the gastric cardia (odds ratio [OR] = 1.3) and noncardia segments (OR = 1.5). This familial tendency, particularly for noncardia gastric tumors, was largely explained by a family history of stomach cancer (OR = 2.5). In addition, a family history of breast cancer was associated with increased risk of esophageal adenocarcinoma (OR = 1.7) or noncardia gastric adenocarcinoma (OR = 1.9). **(Dhillon PK, Farrow DC, Vaughan TL, Chow WH, Risch HA, Gammon MD, Mayne ST, Stanford JL, Schoenberg JB, Ahsan H, Dubrow R, West AB, Rotterdam H, Blot WJ, Fraumeni JF Jr. Family history of cancer and risk of esophageal and gastric cancers in the United States.** ***Int J Cancer*** **2001;93:148-152)**

Nutrient Intake and Risk of Esophageal and Gastric Cancers

A population-based case-control study in Connecticut, New Jersey, and western Washington State found that dietary fiber, beta-carotene, folate, and vitamins C and B6 were significantly inversely associated with esophageal adenocarcinoma, esophageal squamous cell carcinoma, adenocarcinoma of the gastric cardia, and noncardia gastric adenocarcinoma. In contrast, all tumor types were positively associated with dietary cholesterol, animal protein, and vitamin B12. Dietary fat was significantly associated with risk of esophageal adenocarcinoma only (odds ratio [OR] = 2.2, 95 percent CI = 1.3–3.8), and dietary nitrite was associated with noncardia gastric cancer only (OR = 1.7, 95 percent CI = 1.3–2.2). Use of vitamin C supplements was associated with a lower risk for noncardia gastric cancer (OR = 0.6, 95 percent CI = 0.4–0.9). Thus, higher intake of nutrients found primarily in plant-based foods was associated with a reduced risk of adenocarcinomas of the esophagus and gastric cardia, whereas higher intake of nutrients found primarily in foods of animal origin was associated with an increased risk. **(Mayne ST, Risch HA, Dubrow R, Chow WH, Gammon MD, Vaughan TL, Farrow DC, Schoenberg JB, Stanford JL, Ahsan H, West AB, Rotterdam H, Blot WJ, Fraumeni JF Jr. Nutrient intake and risk of subtypes of esophageal and gastric cancer.** ***Cancer Epidemiol Biomarkers Prev*** **2001;10:1055-1062)**

Diet and Genetics in Stomach Cancer

Microsatellite instability (MSI) occurs frequently in sporadic gastric cancer (GC) and may define a distinctive molecular pathway of carcinogenesis. In a study of the role of dietary risk factors in GC according to MSI status, a MSI^+ phenotype was detected in 43 of 126 case subjects (34.1 percent), whereas 83 case subjects were classified as MSI^- (65.9 percent). The risk of MSI^+ tumors was positively associated with high consumption of red meat and meat sauce and negatively associated with consumption of white meat. A positive association was also seen with total protein and nitrite intake, whereas no relationship was found with micronutrient intake. The risk of MSI^+ tumors was especially high among subjects reporting both a positive GC family history and high consumption of red meat (odds ratio = 25.7). For MSI^- tumors, a significant protective effect was associated with frequent consumption of citrus

and other fresh fruit, garlic, legumes, vegetables, and olive oil and with high intake of beta-carotene and other antioxidants and sugar. In contrast, positive associations were seen with protein and sodium intake. (Palli D, Russo A, Ottini L, Masala G, Saieva C, Amorosi A, Cama A, D'Amico C, Falchetti M, Palmirotta R, Decarli A, Costantini RM, Fraumeni JF. Red meat, family history, and increased risk of gastric cancer with microsatellite instability. *Cancer Res* 2001;61:5415-5419)

Glutathione *S*-transferase Genotypes and Stomach Cancer

The relationship between glutathione *S*-transferase genotypes and the risk of stomach cancer was investigated in a population-based case-control study in Warsaw, Poland, where stomach cancer incidence and mortality are among the highest in Europe. There was a 1.5-fold increased risk for stomach cancer (95 percent CI = 0.97–2.3) in patients with the *GSTT1*-null genotype but no evidence of increased risk associated with the *GSTM1*, *GSTM3*, or *GSTP1* genotypes. Furthermore, the stomach cancer risk associated with the *GSTT1*-null genotype was higher in the younger age groups. These results suggest that the *GSTT1*-null genotype may be associated with an increased risk of stomach cancer. (Lan Q, Chow WH, Lissowska J, Hein DW, Buetow K, Engel LS, Ji BT, Zatonski W, Rothman N. Glutathione S-transferase genotypes and stomach cancer in a population-based case-control study in Warsaw, Poland. *Pharmacogenetics* 2001;11:655-661)

LUNG CANCER

Molecular Characteristics of Lung Cancer

Gene expression profiles generated by serial analysis of gene expression (SAGE) were examined by hierarchical clustering in normal lung epithelial cells, squamous cell lung cancers, and lung adenocarcinomas. Separation of normal and tumor tissue, as well as histopathological subtypes, were evident by using the 3,921 most abundant transcript tags and the 115 highly differentially expressed tags. The gene expression patterns observed by SAGE revealed that 115 genes could differentiate between the two tumor types and normal tissue. (Nacht M, Dracheva T, Gao Y, Fujii T, Chen LY, Player A, Akmaev V, Cook B, Dufault M, Zhang M, Zhang W, Guo M, Curran J, Han S, Sidransky D, Buetow K, Madden SI, Jen J. Molecular characteristics of non-small cell lung cancer. *Proc Natl Acad Sci U S A* 2001;98:15203-15208)

MELANOMA

Risk Factors for Melanoma in a Mediterranean Population

In a case-control study of nonfamilial melanoma that included 183 incident case subjects and 179 control subjects in northeastern Italy, the presence of dysplastic nevi (odds ratio [OR] = 4.2, 95 percent CI = 2.4–7.4), low propensity to tan (OR = 2.4, 95 percent CI = 1.1–5.0), light eyes (OR = 2.4, 95 percent CI = 1.1–5.2), and light skin color (OR = 4.1, 95 percent CI = 1.4–12.1) were significantly associated with risk. A chart was developed that identifies melanoma risk associated with combinations of these factors. This chart can be used to identify subjects who would most benefit from preventive measures. The relative risks range from 1.0 to 98.5, depending on the combination of factors present. (Landi MT, Baccarelli A, Calista D, Pesatori A, Fears T, Tucker MA, Land G. Combined risk factors for melanoma in a Mediterranean population. *Br J Cancer* 2001;85:1304-1310)

V126D CDKN2A Founder Mutation in Seven North American Melanoma-prone Families

One of the most common melanoma-related *CDKN2A* mutations reported in North America is the *V126D* mutation. Nine markers surrounding *CDKN2A* in three American and four Canadian families carrying the *V126D* mutation were examined. All seven families had a haplotype consistent with a common ancestor or founder for this mutation. In addition, the mutation appears to have originated 34 to 52 generations ago (1-LOD-unit support interval = 13 to 98 generations). (Goldstein AM, Liu L, Sherman MG, Hogg D, Tucker MA, Struewing JP. A common founder for the *V126D CDKN2A* mutation in seven North American melanoma-prone families. *Br J Cancer* 2001;85:527-530)

Germline Mutations in Sporadic Melanoma

One hundred persons with multiple primary melanomas, but without any known melanoma cases within their families, were evaluated for germline mutations in the two melanoma-predisposing genes identified to date, *CDKN2A* and *CDK4* exon 2. Nine patients (9 percent) had germline mutations in *CDKN2A*, whereas none carried germline mutations in exon 2 of *CDK4*. Seven patients displayed a recurrent missense mutation already described in more than 20 melanoma-prone families (G101W), one carried a missense mutation never reported to date (P114S), and the last was a carrier of a six-base pair insertion at nucleotide 57 resulting in a duplication of codons 18 and 19. To ascertain whether the G101W was a mutational hot spot for *de novo* mutations or a common founder mutation, eight microsatellite markers flanking the *CDKN2A* gene were genotyped. The results suggested that *de novo* germline *CDKN2A* mutations associated with multiple primary melanomas are rare. (Auroy S, Avril M-F, Chompret A, Pham D, Goldstein AM, Bianchi-Scarra G, Frebourg T, Joly P, Spatz A, Rubino C, Demenais F, Bressac-de Paillierets B, French Hereditary Melanoma Study Group. Sporadic multiple primary melanoma cases: *CDKN2A* germline mutations with a founder effect. *Genes Chromosomes Cancer* 2001;32:195-202)

METHODS

Bivariate Cure-mixture Approach for Modeling Familial Association in Diseases

For modeling correlation in familial diseases with variable age at onset, a bivariate model was proposed that incorporates two types of pairwise association, one between the lifetime risk or the overall susceptibility of two individuals, and one between the age at onset of two susceptible individuals. For estimations, a two-stage estimation procedure similar to that of Shih (Biometrics 1998;54:1115-1128) was considered. The properties of the estimators were evaluated through simulations, and performance was compared with that from a bivariate survival model that permits correlation between age at onset only. The methodology was applied to breast cancer, using the kinship data from the Washington Ashkenazi Study. Other applications of the proposed method in the area of cure modeling are possible. **(Chatterjee N, Shih J. A bivariate cure-mixture approach for modeling familial association in diseases. *Biometrics* 2001;57:779-786)**

Effects of Assumptions on Likelihood Methods for Estimating Penetrance in Kin-cohort Studies

The effects of violations of key assumptions on likelihood-based inference methods for estimating prevalence in kin-cohort studies were examined. Serious overestimates of disease risk (penetrance) and allele frequency can result if more persons with than without affected relatives volunteer to be probands, and if probands give false-positive reports of disease. Conversely, penetrance will be underestimated if probands fail to report all the disease present among their relatives. Sources of familial disease aggregation other than the gene under study result in overestimates of the penetrance in mutation carriers, underestimates of penetrance in noncarriers, and overestimates of allele frequency. Unless sample sizes are quite large, confidence intervals based on the Wald procedure can have subnominal coverage; limited numerical studies indicate that likelihood ratio-based confidence intervals perform better. **(Gail MH, Pee D, Carroll R. Effects of violations of assumptions on likelihood methods for estimating the penetrance of an autosomal dominant mutation from kin-cohort studies. *J Stat Plann Inference* 2001;96: 167-177)**

Association and Aggregation Analysis Using Kin-cohort Designs

A method for analyzing kin-cohort data was developed to simultaneously estimate the age-specific cumulative risk of a disease among carriers and noncarriers of mutations and the gene-adjusted residual familial aggregation or correlation of the disease. A semiparametric modeling approach was used, wherein the marginal cumulative risks corresponding to the carriers and noncarriers are treated nonparametrically and the residual familial aggregation is described parametrically by a class of bivariate failure-time models known as copula models. A simple and robust two-stage method was developed for estimation and applied to data from the Washington Ashkenazi Study. **(Chatterjee N, Shih J, Hartge P, Brody L, Tucker M, Wacholder S. Association and aggregation analysis using kin-cohort designs with applications to genotype and family history data from the Washington Ashkenazi Study. *Genet Epidemiol* 2001;21:123-138)**

Limitations of the Case-only Design for Identifying Case-control Interactions

The case-only design, which requires only diseased subjects, allows for estimation of multiplicative interactions between factors known to be independent in the study population. Estimates of gene-environment interactions are very efficient relative to estimates obtained with a case-control study under the assumption of independence between the genetic and environmental factors. The robustness of this procedure to uncertainty about the independence assumption was explored. With use of simulations, it was demonstrated that inferences about the multiplicative interaction with the case-only design can be highly distorted when there is departure from the independence assumption. **(Albert PS, Ratnasinghe D, Tangrea J, Wacholder S. Limitations of the case-only design for identifying gene-environment interactions. *Am J Epidemiol* 2001;154:687-693)**

Collection of Genomic DNA by Buccal Cytobrush and Mouthwash

The buccal cytobrush and the alcohol-containing mouthwash protocols for collecting DNA by mail, as well as several DNA extraction techniques, were evaluated. DNA isolated from either cytobrush or mouthwash samples from adults is adequate for a wide range of PCR-based assays, but a single mouthwash sample provides substantially larger amounts and higher-molecular-weight DNA than two cytobrush samples do. **(Garcia-Closas M, Egan KM, Abruzzo J, Newcomb PA, Titus-Ernstoff L, Franklin T, Bender PK, Beck JC, Le Marchand L, Lum A, Alavanja M, Hayes RB, Rutter J, Buetow K, Brinton LA, Rothman N. Collection of genomic DNA from adults in epidemiological studies by buccal cytobrush and mouthwash. *Cancer Epidemiol Biomarkers Prev* 2001;10:687-696)**

OCCUPATIONAL EXPOSURES

Pesticides and Non-Hodgkin's Lymphoma

Data from three population-based case-control studies conducted in Kansas, Nebraska, Iowa, and Minnesota were pooled to evaluate the relationship between pesticide use and non-Hodgkin's lymphoma (NHL) among white male farmers. Use of organophosphate pesticides was associated with a significant, 50 percent increase in the

risk of NHL, but direct interviews showed a significantly lower risk (odds ratio [OR] = 1.2) than proxy interviews did (OR = 3.0). In direct interviews, the risk of small lymphocytic lymphoma increased with diazinon use (OR = 2.8) after adjustment for other pesticide exposures. **(Waddell BL, Zahm SH, Baris D, Weisenburger DD, Holmes F, Burmeister LF, Cantor KP, Blair A. Agricultural use of organophosphate pesticides and the risk of non-Hodgkin's lymphoma among male farmers (United States). *Cancer Causes Control* 2001;12:509-517).**

Farmers who had ever used carbamate pesticides had a 30 to 50 percent increase in the risk of NHL, whereas farmers who had never used them showed no increased risk. Analyses for individual carbamate pesticides found a more consistent association with Sevin than with carbofuran, butylate, or *S*-ethyl dipropylthiocarbamate plus protectant. Among farmers using Sevin, the risk of NHL was limited to those who personally handled the product, those who first used the product at least 20 years before their disease diagnosis, or those who used the product for seven years or more. These associations persisted after adjustment for other major classes of pesticides. **(Zheng TZ, Zahm SH, Cantor KP, Weisenburger DD, Zhang YW, Blair A. Agricultural exposure to carbamate pesticides and risk of non-Hodgkin lymphoma. *J Occup Environ Med* 2001;43:641-649)**

Diesel Engine Emissions and Cancer

In a large record-linkage study from Sweden, men exposed to diesel emissions, based on job and industry titles in the 1960 census, experienced an increased risk of lung cancer (relative risk = 1.3 for high-intensity versus no exposure). The risk was higher for squamous cell carcinoma of the lung than for other histological types. A small but significant increase in risk was found for cancer of the stomach (standardized incidence ratio [SIR] = 1.06), pancreas (SIR = 1.05), larynx (SIR = 1.09), and kidney (SIR = 1.06), but there was no clear trend according to either probability or intensity of exposure. A significantly increased risk of oral or pharyngeal cancer (SIR = 1.64) and cervical cancer (SIR = 1.48) was present among women, with a suggestion of a dose-response relationship. There was no increased risk of bladder cancer in either gender. **(Boffetta P, Dosemeci M, Gridley G, Bath H, Moradi T, Silverman D. Occupational exposure to diesel engine emissions and risk of cancer in Swedish men and women. *Cancer Causes Control* 2001;12:365-374)**

OVARIAN CANCER

Risk Modifiers for Ovarian Cancer among *BRCA1* or *BRCA2* Carriers

The effects of parity and use of oral contraceptives (OCs) on the risk of ovarian cancer among *BRCA1* and *BRCA2* carriers and noncarriers were estimated in a case-control study among Israeli women. Of 751 control subjects who underwent mutation analysis, 13 (1.7 percent) had a *BRCA1* or *BRCA2* mutation, whereas 244 of 840 women with ovarian cancer (29.0 percent) had a *BRCA1* or *BRCA2* mutation. Overall, each additional birth and each additional year of OC use lowered the risk of ovarian cancer, as expected. Additional births were protective in separate analyses of carriers and noncarriers, but use of OCs appeared to reduce the risk only in noncarriers; among carriers, the reduction in the odds of ovarian cancer was 12 percent per birth and 0.2 percent per year of OC use. The risk of ovarian cancer among carriers of a *BRCA1* or *BRCA2* mutation decreased with each birth but not with increased duration of OC use. These data suggest that it is premature to use OCs for the chemoprevention of ovarian cancer in carriers of such mutations. **(Modan B, Hartge P, Hirsh-Yechezkel G, Chetrit A, Lubin F, Beller U, Ben-Baruch G, Fishman A, Menczer J, Struewing JP, Tucker MA, Wacholder S, for the National Israel Ovarian Cancer Study Group. Parity, oral contraceptives, and the risk of ovarian cancer among carriers and noncarriers of a *BRCA1* or *BRCA2* mutation. *N Engl J Med* 2001;345: 235-240)**

PANCREATIC CANCER

Helicobacter pylori and Risk of Pancreatic Cancer

The association of *Heliocobacter pylori* carriage and exocrine pancreatic cancer was evaluated in a study of 121 case subjects and 226 control subjects within the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study of male Finnish smokers. Levels of immunoglobulin G antibodies to *H. pylori* whole-cell and $CagA^+$ antigens from stored baseline sera were measured by enzyme-linked immunosorbent assay. Seroprevalence of *H. pylori* was 82 percent among case subjects and 73 percent among control subjects. Compared with seronegative subjects, those with *H. pylori* were at significantly elevated risk of pancreatic cancer (odds ratio = 1.9, 95 percent CI = 1.1–3.3), as were those with the $CagA^+$ strains (odds ratio = 2.0, 95 percent CI = 1.1–3.7), suggesting a possible role for *H. pylori* in the development of exocrine pancreatic cancer. **(Stolzenberg-Solomon RZ, Blaser MJ, Limburg PJ, Perez-Perez G, Taylor PR, Virtamo J, Albanes D. *Helicobacter pylori* seropositivity as a risk factor for pancreatic cancer. *J Natl Cancer Inst* 2001;93:937-941)**

PROSTATE CANCER

Polymorphic Markers in the *SRD5A2* Gene and Prostate Cancer Risk

The activity of the steroid 5-alpha-reductase type II enzyme (encoded by the *SRD5A2* gene) may be associated with prostate cancer risk. We evaluated the relationship of four polymorphic markers in the *SRD5A2* gene (A49T,

V89L, R227Q, and a $[TA]_n$ dinucleotide repeat) with prostate cancer risk in a study of 191 incident case subjects and 304 control subjects in China. Serum androgen levels were also measured. For the V89L marker, relative to men with the *VV* genotype, those with the *LL* genotype had a nonsignificant, 12 percent reduced risk (odds ratio = 0.9, 95 percent CI = 0.5–1.5). In addition, men with the *LL* genotype had significantly higher serum levels of testosterone and significantly lower serum levels of 5-alpha-androstane-3-alpha, 17-beta-diol glucuronide than did men with other genotypes. Compared with men homozygous for the $(TA)_0$ allele of the $(TA)_n$ marker, men heterozygous for the $(TA)_0$ allele had a modest, nonsignificant risk reduction (odds ratio = 0.7, 95 percent CI = 0.4–1.1), along with significantly higher serum dihydrotestosterone levels. **(Hsing AW, Chen C, Chokkalingam AP, Gao YT, Dightman DA, Nguyen HT, Deng J, Cheng J, Sesterhenn IA, Mostofi FK, Stanczyk FZ, Reichardt JK. Polymorphic markers in the *SRD5A2* gene and prostate cancer risk: A population-based case-control study. *Cancer Epidemiol Biomarkers Prev* 2001;10:1077-1082)**

RADIATION

Cancer Deaths after Nasopharyngeal Radium Irradiation

A retrospective cohort study of 5,358 subjects exposed to nasopharyngeal radium irradiation during childhood as treatment for otitis serosa and 5,265 nonexposed subjects was conducted. All subjects were treated at nine ear, nose, and throat clinics in the Netherlands from 1945 through 1981. There was no excess mortality from cancers of the head or neck area among exposed subjects. However, there were excess deaths from cancers of lymphoproliferative or hematopoietic origin (standardized mortality ratio [SMR] = 1.9)—mainly from non-Hodgkin's lymphoma (SMR = 2.6). The study found no evidence that breast cancer deaths were less than expected (SMR = 1.7), in contrast to an earlier study. **(Ronckers CM, Land CE, Verduijn PG, Hayes RB, Stovall M, van Leeuwen FE. Cancer mortality after nasopharyngeal radium irradiation in the Netherlands: A cohort study. *J Natl Cancer Inst* 2001;93:1021-1027)**

VIRUSES

Effects of Three Specific Alleles on HIV-1 Disease Progression

To examine postulated associations of genetic alleles with HIV-1 disease progression, a meta-analysis of studies from the United States, Europe, and Australia was conducted. Both the *CCR5-Δ32* and *CCR2-64I* alleles were associated with decreased risk of progression to AIDS (relative hazard among seroconverters = 0.7 and 0.8, respectively, $p = 0.01$ for both), decreased risk of death (relative hazard among seroconverters = 0.6 and 0.7, respectively, $p < 0.05$ for both), and lower HIV-1 RNA level after seroconversion (difference of –0.2 and –0.1 log(10), respectively, $p < 0.05$ for both). Whereas the *CCR5-Δ32* and *CCR2-64I* alleles had a strong protective effort on progression of HIV-1 infection, *SDF-1 3'A* homozygosity carried no such protection. **(Ioannidis JPA, Rosenberg PS, Goedert JJ, Ashton LJ, Benfield TL, Buchbinder SP, Coutinho RA, Eugen-Olsen J, Gallart T, Katzensein TL, Kostrikis LG, Kuipers H, Louie L, Mallal SA, Margolick JB, Martinez OP, Meyer L, Michael NL, Operskalski E, Pantaleo G, Rizzardi GP, Schuitemaker H, Sheppard HW, Stewart GJ, Theodorou ID, Ullum H, Vicenzi E, Vlahov D, Wilkenson D, Workman C, Zagury J-F, O'Brien TR, for the International Meta-Analysis of HIV Host Genetics. Effects of *CCR5-Δ32*, *CCR2-64I*, and *SDF-1 3'A* alleles on HIV-1 disease progression: An international meta-analysis of individual-patient data. *Ann Intern Med* 2001;13:782-795)**

Malignancies in Persons with AIDS and Kaposi's Sarcoma

Kaposi's sarcoma (KS), common among persons with AIDS, is caused by the KS herpesvirus (KSHV), but whether KSHV causes other malignancies is uncertain. AIDS and cancer registries in the United States were used to measure the incidence of specific malignancies in persons with AIDS-related KS compared with other persons with AIDS. Only immunoblastic lymphoma was significantly associated with KS, suggesting that KSHV is involved in at least some immunoblastic lymphomas. **(Engels EA, Rosenberg PS, Frisch M, Goedert JJ. Cancers associated with Kaposi's sarcoma (KS) in AIDS: A link between KS herpesvirus and immunoblastic lymphoma. *Br J Cancer* 2001;85:1298-1303)**

Prevalence of Human Herpesvirus 8 Antibodies in Denmark

To study the prevalence of human herpesvirus 8 (HHV8) infection before the HIV epidemic, sera from 641 persons who attended an outpatient clinic for a sexually transmitted disease in Copenhagen, Denmark, from March 1976 through February 1977 were examined for HHV8 antibodies. Overall, 27 patients (4.2 percent) had HHV8 antibodies, and the prevalence of antibodies increased with patient's age. Originating from a classic Kaposi's sarcoma-endemic area was associated with a 15.7-fold increased likelihood of having HHV8 antibodies (95 percent CI = 5.0–45.5), while a history of gonorrhea was associated with a 3.4-fold increased likelihood (95 percent CI = 1.4–10.4). Along with other lines of evidence, these data suggest that the prevalence of HHV8 antibodies was elevated in homosexual men before the onset of the HIV epidemic. **(Hjalgrim H, Lind I, Rostgaard K, Melbye M, Frisch M, Stossel A, Reimann K, Biggar RJ, Whitby D. Prevalence of human herpesvirus 8 antibodies in young adults in Denmark (1976–1977). *J Natl Cancer Inst* 2001;93:1569-1571)** ■

DCEG PEOPLE IN THE NEWS


Dr. Gilbert Beebe

Seven DCEG investigators received NIH Merit Awards in September. **Gilbert Beebe, Ph.D.,** Scientist Emeritus, was recognized for his studies of radiation-related cancer risk from the Chornobyl reactor accident. **Montserrat Garcia-Closas, M.D., Dr.P.H.,** of the Environmental Epidemiology Branch (EEB), was cited for her research that has defined methods for assessing gene-environment interactions within the context of epidemiologic studies. EEB's **Ann Hsing, Ph.D.,** was recognized for research that has provided important clues to explain the substantial racial differences in prostate cancer risk. **Peter Inskip, Sc.D.,** of the Radiation Epidemiology Branch (REB), was cited for his research on the relationship between cellular telephone use and brain tumors in adults. **Mark Schiffman, M.D., M.P.H.,** of EEB, and **Robert Tarone, Ph.D.,** of the Biostatistics Branch (BB), were recognized along with Dr. Diane Solomon of NCI's Division of Cancer Prevention for leadership of the ASCUS/LSIL Triage Study to optimize management of cervical cytology abnormalities. **Jimmie B. Vaught, Ph.D.,** of the Office of the Director, was cited for his important contributions in developing methods and procedures to improve the management of DCEG's biorepositories.


Dr. Montserrat Garcia-Closas


Dr. Ann Hsing


Dr. Peter Inskip


Dr. Jimmie B. Vaught


Dr. Louise Brinton

In October, three DCEG researchers received NIH Quality of Work Life Awards. EEB Chief **Louise Brinton, Ph.D.,** was recognized for her successful reshaping of EEB from 1996 to the present, which has led to greatly improved staff satisfaction and major improvements in administrative efficiency. **Martha Linet, M.D., M.P.H.,** of REB, was recognized for her efforts to strengthen communications, provide a forum for discussion, and offer training in areas of particular relevance to women scientists in her role as the DCEG Women Scientists' Advisor. **Thomas O'Brien, M.D.,** of the Virology Epidemiology Branch, was honored for his contributions as the Chair of the DCEG Committee of Scientists to improve communication, enhance the scientific environment, and provide career development opportunities within DCEG.


Dr. Martha Linet


Dr. Thomas O'Brien


Dr. Neil Caporaso

Neil Caporaso, M.D., of the Genetic Epidemiology Branch (GEB), received an Outstanding Service Medal from the PHS Commissioned Corps for "Leadership in defining the biologic basis for nicotine addiction."


Dr. Nilanjan Chatterjee

Nilanjan Chatterjee, Ph.D., has been appointed as a new tenure-track investigator in BB. He received his doctorate in statistics from the University of Washington in 1999. Since joining DCEG, he has worked on estimation of the penetrance of genetic mutations from data in kin-cohort designs. He has recently developed a two-stage regression analysis for case-control epidemiologic data that can be used to investigate the effect of risk factors on various case characteristics.

This year's winners of the NIH 2001 Fellows Award for Research Excellence (FARE) competition included three DCEG fellows. The winning entry of EEB member **Anand Chokkalingam, Ph.D.,** was entitled "Vitamin D Receptor Gene Polymorphisms, Insulin-like Growth Factors, and Prostate Cancer: A Population-based Case-control Study in China." **Ulrike Peters, Ph.D.,** of the Nutritional Epidemiology Branch, won the award for her abstract, "Dietary Fiber and Colorectal Adenoma—Data from the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial." The research of GEB member **Rose Yang, Ph.D.,** was titled "A Familial Chordoma Locus Is Linked to Chromosome 7q33." The fellows each received a $1,000 stipend to attend a scientific meeting to present their abstracts and will also be asked to present at a FARE poster session. They will serve as judges for FARE 2003.


Dr. Ulrike Peters


Dr. Rose Yang

In December, **Joseph F. Fraumeni, Jr., M.D.,** DCEG Director, presented the 135th Cutter Lecture on Preventive Medicine at the Harvard School of Public Health. His talk was entitled, "Genes and the environment in cancer causation: Epidemiologic opportunities." In November, Dr. Fraumeni received the First Amgen Visiting Professorship by the Yale Cancer Center. And in October, he was a guest of honor at the "Lunch With Leaders" program sponsored by the Department of Epidemiology at the Johns Hopkins University Bloomberg School of Public Health.


Dr. Lynn Goldin

GEB member **Lynn R. Goldin, Ph.D.,** recently participated in teaching a course in Cambridge, UK, entitled, "Human Genome Analysis: Genetic Analysis of Multifactorial Diseases," sponsored by the Wellcome Trust. Her lecture focused on strategies for improving the power of gene detection in complex diseases.

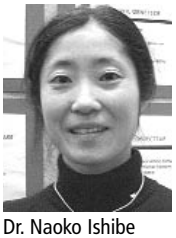

Ms. Gloria Gridley

Gloria Gridley, M.S., of BB, gave an invited talk in October before the Hispanic Dental Association in Philadelphia. The title was "The role of dietary factors in the etiology of oral and pharyngeal cancers."


Dr. Allan Hildesheim

Allan Hildesheim, Ph.D., of EEB, was the invited speaker for the January 18th NIH Director's Seminar Series. Dr. Hildesheim's talk, "Human papillomavirus (HPV) and cervical cancer: The road from etiological understanding to preventive strategies," told the story of the scientific work done to elucidate the association between HPV and cervical cancer. He began by examining the initial efforts to establish an etiologic role for the virus in cervical cancer and went on to cover current endeavors to develop better diagnostic tools and the start of HPV vaccine trials to prevent cervical cancer. Dr. Hildesheim also spoke of the role he has played in this research, including past and ongoing studies in Guanacaste, Costa Rica.

Ann Hsing, Ph.D., of EEB, served as lead editor of a recent issue of *Epidemiologic Reviews* devoted to prostate cancer. The volume includes articles on more than 30 topics, including descriptive epidemiology, natural history, occupation, medical history, gene-environment interactions, and prevention and control. Dr. Hsing authored an article on "Hormones and prostate cancer: what's next?" and with BB member **Susan Devesa, Ph.D.,** coauthored an article on trends and patterns of prostate cancer. **Richard Hayes, D.D.S., Ph.D.,** of the Occupational Epidemiology Branch (OEB), contributed an article on gene-environment interrelations and co-authored another article about alcohol. **James Goedert, M.D.,** of the Viral Epidemiology Branch, co-authored an article on sexual behavior and evidence suggesting an infectious cause of prostate cancer.


Dr. Naoko Ishibe

Naoko Ishibe, Sc.D., has been appointed a tenure-track investigator in GEB. Shortly after receiving her doctor of science degree in epidemiology and environmental health from the Harvard School of Public Health in 1997, Dr. Ishibe became a postdoctoral fellow in the Cancer Genetics Training Program in DCEG. She has been involved in research on von Hippel-Lindau disease and on the causes and natural history of familial chronic lymphocytic leukemia. Dr. Ishibe is also an accomplished athlete and was recently selected to the U.S. National Track and Field Team. She competed in a road relay in Chiba, Japan, in November.


Dr. James Lacey

James Lacey, Jr., Ph.D., was selected for a tenure-track position in EEB. Dr. Lacey has been in DCEG as a postdoctoral fellow since completing his Ph.D. at the University of Michigan in 1998. His research has focused on hormonal carcinogenesis involving tumors of the breast, endometrium, cervix, and ovary. He is also leading a large cohort study to define the interrelationship of bone density, genetic factors, and endogenous hormones as predictors of subsequent breast, endometrial, and colorectal cancer risk.

At the NCI Awards Ceremony in September, two GEB members received Achievement Medals from the PHS Commissioned Corps. LCDR **Mary Lou McMaster, M.D.,** was recognized "for increasing our understanding of the etiology and clinical manifestations of several familial cancers," while **CAPT Mary Fraser, R.N., M.A.,** was recognized "for outstanding coordination of the GEB site visit."


Dr. Elizabeth Maloney

Elizabeth Maloney, Dr. P.H., a staff scientist in the Viral Epidemiology Branch, successfully defended her doctoral thesis at the Uniformed Services University of the Health Sciences (USUHS). Dr. Maloney's thesis focused on a cohort study of the health effects of human T cell-lymphotropic virus type I (HTLV-I) infection in Jamaican children. She found that, compared

with uninfected children, HTLV-I-infected children had significantly higher incidence rates of eczema, seborrheic dermatitis, and persistent hyperreflexia and nonsignificantly elevated rates of severe anemia, lymphadenopathy, and abnormal lymphocytes. Among infected children, those with seborrheic dermatitis and severe anemia had an approximately twofold higher HTLV-I proviral load than children without these conditions did. Her academic advisor, Terry Thomas, Ph.D., of the Radiation Epidemiology Branch, was a faculty member at USUHS before joining DCEG.


Dr. Robert Miller

The University of Pennsylvania School of Medicine recently honored **Robert W. Miller, M.D., Dr.P.H.,** DCEG Scientist Emeritus, as a Distinguished Alumnus.


Dr. Ruth Pfeiffer

Ruth Pfeiffer, Ph.D., has been appointed to a tenure-track position in BB. She received her doctorate in mathematical statistics from the University of Maryland in 1998. Since joining DCEG in 1999 as a postdoctoral fellow, she has worked on estimation of covariate effects from family data, taking into account ascertainment. She has also developed mixture models that can aid in analyzing serologic data in the absence of a gold standard. Her future plans include assessing power and sample sizes for association studies based on genetic markers, rather than candidate genes, and extending the mixture model to longitudinal data. Dr. Pfeiffer is also developing models of absolute risk for colon cancer and other cancers.


Dr. Cecile Ronckers

Cecile Ronckers, Ph.D., an REB visiting fellow, was chosen to receive the Young Investigator Travel Award from the Radiation Research Society. Dr. Ronckers will present an abstract entitled "Late Health Effects of Nasopharyngeal Radium Irradiation: Cancer Incidence" at the annual Society meeting, which will be held April 20–24, 2002, in Reno, Nevada.

EEB member **Mark Schiffman, M.D., M.P.H.,** was recognized as an NCI Mentor of Merit by the NCI Fellowship Office. Dr. Schiffman was also elected to the Johns Hopkins Society of Scholars, which honors former postdoctoral fellows and junior or visiting faculty who have gained distinction in their fields.


Dr. Rashmi Sinha


Dr. Elizabeth Snyderwine

Rashmi Sinha, Ph.D., of NEB, and **Elizabeth Snyderwine, Ph.D.,** of the NCI's Center for Cancer Research, organized and chaired the 8th International Conference on Carcinogenic/Mutagenic *N*-Substituted Aryl Compounds, which was held November 12–14, 2001, in Washington, DC. The conference, held every three years, brought together researchers from 14 countries and 5 continents who share a mutual interest in understanding the role arylamines play in carcinogenesis. Many DCEG scientists participated, including OEB's **Nathaniel Rothman, M.D., M.P.H., M.H.S.,** who spoke on "NAT2, aromatic amines, and bladder cancer," and EEB's **Montserrat Garcia-Closas, M.D., Dr.P.H.,** who spoke on "Methodological challenges to the study of genetic susceptibility to dietary sources of *N*-aryl compounds in epidemiological studies of cancer."


Dr. Margaret Tucker

Margaret A. Tucker, M.D., GEB Chief, recently gave invited talks at the International Symposium on Radiation and Homeostasis in Kyoto, Japan; at the "Carcinogenesis and Cancer Prevention: Non-Melanoma and Melanoma Skin Cancer" meeting at the University of California at Irvine; and at the "Technological Innovation in a Changing Medical Marketplace" meeting at the National Academy of Sciences, Washington, DC.

In November, DCEG Deputy Director Shelia Zahm, Sc.D., was the lead speaker at the symposium "Evolution of Exposure Assessment for Epidemiologic Research at the National Cancer Institute," at a meeting of the International Society for Exposure Analysis in Charleston, South Carolina. Other DCEG staff members—OEB's **Mary Ward, Ph.D., Mustafa Dosemeci, Ph.D., Joseph Coble, Sc.D.,** and **Jay Nuckols, Ph.D.,** and REB's **Ruth Kleinerman, M.P.H.**—presented papers on exposure assessment in environmental, occupational, and radiation studies. The session was organized and chaired by **Joanne Colt, M.S., M.P.H.,** of OEB. ■

COMINGS … GOINGS


Dr. Sean Altekruse

Sean Altekruse, D.V.M., Ph.D., M.P.H., joined the Environmental Epidemiology Branch (EEB) as a Staff Scientist in September. He is a board-certified veterinarian (University of Georgia, 1987) and a PHS Commander. During the past decade, he worked at the Centers for Disease Control and Prevention in Atlanta and at the Food and Drug Administration in Washington, DC. This year, Dr. Altekruse completed the PHS Epidemiology Fellowship Program and was awarded a Ph.D. from Virginia Polytechnic Institute. He will coordinate the Costa Rican human papillomavirus vaccine trial with Dr. Allan Hildesheim and Dr. Mark Schiffman.


Dr. Michelle Althuis

Michelle Althuis, Ph.D., recently joined EEB as a postdoctoral fellow. She received a master's degree in organic chemistry from the Johns Hopkins University and a doctoral degree in epidemiology from the University of Maryland. For her dissertation, she conducted a community-based study assessing the prevalence of endometrial cancer screening among women with breast cancer. More recently, she has worked in the design and analysis of clinical trials.


Ms. Elizabeth Brown

Elizabeth E. Brown joined the Viral Epidemiology Branch in July as a predoctoral fellow. She received her B.S. from the University of Oregon and has completed course work for a Ph.D. in epidemiology from the Johns Hopkins University Bloomberg School of Public Health. For her dissertation, she is working with Drs. James Goedert, Denise Whitby, and Stephen Chanock on the effects of cytokines and cytokine gene polymorphisms on the risk of classic Kaposi's sarcoma.


Dr. Abhijit Dasgupta

Abhijit Dasgupta, Ph.D., joined the Biostatistics Branch (BB) in September as a postdoctoral fellow after receiving his doctorate in biostatistics from the University of Washington. He is working with Dr. Sholom Wacholder on estimating penetrance of *BRCA1* and *BRCA2* mutations for ovarian cancer and on expression array studies of cervical lesions.

Omur Elci, M.D., Ph.D., departed the Occupational Epidemiology Branch (OEB) in September for a position at the National Institute for Occupational Safety and Health in Morgantown, West Virginia. Dr. Elci had been a visiting fellow since 1999, investigating occupational and environmental risk factors for laryngeal cancer.

Dan Grauman, M.S., recently transferred from BB to the Division of Cancer Control and Population Sciences. Mr. Grauman played a critical role in developing the user-friendly web site for cancer maps and mortality data and is now developing material for the web site of his new Division.


Dr. Dupont Guerry

DuPont Guerry IV, M.D., is spending a sabbatical year in the Genetic Epidemiology Branch. Dr. Guerry is a professor of hematology and oncology at the University of Pennsylvania Health Center, and director of the world-famous Pigmented Lesion Clinic of the University of Pennsylvania Cancer Center's Melanoma Program. He has collaborated on studies of melanoma with DCEG investigators for over 20 years. He is analyzing data from a case-control study of melanoma and is helping to develop protocols for familial lymphoproliferative diseases.


Dr. Jose Jeronimo

Jose Jeronimo Guibovich, M.D., joined EEB as a research fellow. Dr. Jeronimo received his M.D. in 1989 from the Federico Villarreal University in Lima, Peru, and subsequently completed a residency in general and oncologic surgery in 1995 and a fellowship in gynecologic oncology in 1996. In addition to his clinical duties, he actively participated in prevention research, including collaboration with the Pan American Health Organization on visual screening for cervical cancer precursors. Dr. Jeronimo's research will focus on studying the visual natural history of cervical cancer with the use of archived digital and photographic images from EEB investigations. The visual data will be merged with corresponding microscopic and virologic data to explore issues such as lesion clonality and topography.


Dr. Wonjin Lee

Wonjin Lee, M.D., Ph.D., joined OEB as a visiting fellow in October. Dr. Lee was trained in occupational and environmental medicine at Korea University. He spent the past two years at the International Agency for Research

on Cancer working on a mortality study in the pulp and paper industry and on a molecular epidemiology project evaluating the relationship between genetic polymorphisms and lung cancer. Dr. Lee will conduct research on pesticides in relation to cancer risk.


Ms. Judith Lindley

Ms. Judy Lindley joined the Administrative Resource Center as an administrative technician. Judy comes from Oklahoma, where she worked as a program assistant for the General Services Administration. She has experience in both personnel and administration.

Aparna Mohan, M.D., Ph.D., a postdoctoral fellow in the Radiation Epidemiology Branch (REB), recently left DCEG to join the Center for Biologics Evaluation and Research at the Food and Drug Administration.


Dr. Lee Moore

In August, **Lee Moore, Ph.D.,** joined OEB as a tenure-track investigator. Dr. Moore has a doctorate in epidemiology from the University of California at Berkeley. Her research has focused on the relationship of inorganic arsenic with cancer. At DCEG, Dr. Moore will be investigating gene-environment interactions in the development of kidney cancer in Eastern Europe and the molecular epidemiology of arsenic and bladder cancer in New England.

After two years as an Epidemiology Program Specialist, **Amy Pickard, M.P.H.,** left EEB in August to begin doctoral dissertation work at the University of Michigan.


Dr. Ehab Rabaa

Ehab Rabaa, M.D., M.P.H., recently joined the Viral Epidemiology Branch as a postdoctoral fellow. He trained in medicine at Tishreen University in Lattakia, Syria, and received his M.P.H. from the University of New Mexico in Albuquerque. At DCEG, Dr. Rabaa will collaborate with Dr. James Goedert on hepatitis C virus and avian leukosis virus, and with Dr. Robert Biggar and Dr. Elizabeth Maloney on studies of human T-cell lymphotrophic virus type II.


Ms. Rachelle Ragland-Green

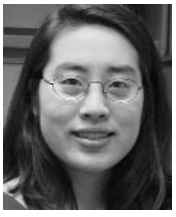
Ms. Rachelle Ragland-Greene joined the Administrative Resource Center as an administrative technician. Her previous work experience includes jobs in marketing and human resources in the private sector. Since joining NCI in the fall, she has completed several Federal training courses, including use of DELPRO and government travel.


Ms. Preetha Rajaraman

Preetha Rajaraman joined REB in December as a predoctoral fellow to work on a study of occupational exposures and brain tumors. Ms. Rajaraman is a doctoral student at the Johns Hopkins University Bloomberg School of Public Health. Her mentors are Dr. Peter Inskip and Dr. Patricia Stewart.


Dr. Sowmya Rao

Sowmya Rao, Ph.D., who received her doctorate in biostatistics from Boston University, is a BB postdoctoral fellow. Dr. Rao plans to develop statistical methods for analyzing health surveys to answer epidemiologic questions. She will also develop epidemiologic and statistical methods for analyzing associations between radiation exposure and cancer in cohort studies.


Ms. Lori Sakoda

Lori Sakoda, M.P.H., joined EEB in November as an epidemiology program specialist. Originally from Hawaii, she received an A.B. in psychology from Stanford University and an M.P.H. in epidemiology and biostatistics from the University of California at Berkeley. For the last two years, she was employed by Northern California Cancer Center and Kaiser Permanente Oakland, where she examined dietary, anthropometric, and hormone-related risk factors for thyroid and breast cancer among ethnically diverse populations, and conducted research comparing the diagnostic yield between various colorectal cancer screening strategies.


Dr. Adonina Tardon

Adonina Tardón-García, M.D., Ph.D., has joined OEB as a guest researcher. She has a medical degree from the Universidad Complutense de Madrid and a Ph.D. in epidemiology from Universidad de Oviedo, Spain. During her sabbatical year at NCI, she will collaborate with DCEG investigators in the analysis of data from the recently completed case-control study of bladder cancer in Spain.


Dr. Jorge Toro

Jorge Toro, M.D., has joined the Genetic Epidemiology Branch as a tenure-track investigator. Dr. Toro graduated with honors from the State University of

New York at Buffalo School of Medicine in 1992. In 1997, he came to the NIH under a fellowship and completed his residency in dermatology. His primary research interest is hereditary diseases of the skin, from clinical presentation to gene identification, characterization, and mutation detection. He defined for the first time the dermatological findings of Hermansky-Pudlak syndrome and recently described the association of Birt-Hogg-Dubé syndrome with renal cancer. Dr. Toro will continue his study of these syndromes, pursue an interest in gamma-delta T-cell lymphoma, and explore the manifestations and implications of cutaneous leiomyomatosis.


Ms. Marianne Vidal

Marianne Vidal, M.S., a special volunteer from the Institute for Protection and Nuclear Safety (IPSN) in Paris, will spend one year with REB's Chornobyl Research Unit, assisting in dosimetry activities to estimate the ^{131}I thyroid dose received by persons in Belarus and Ukraine during the Chornobyl nuclear power accident. ■

IN MEMORIAM

Susan Sieber, Ph.D., who served as DCEG's Deputy Director from 1995 through 1997, passed away on January 22, 2002, after an extended illness. Dr. Sieber spent her professional career in public service, retiring in September 2001 after 30 years at NCI.

Her career at NCI began in 1971 when she joined the Laboratory of Chemical Pharmacology as a postdoctoral fellow after completing her Ph.D. in pharmacology at George Washington University. In 1976, she was appointed Chief of the Pharmacology and Experimental Therapeutics Section.

Dr. Sieber became well known to many in DCEG when she was selected Deputy Director of the Division of Cancer Etiology, the predecessor to the DCEG, in 1983. Following the establishment of DCEG in 1995, she agreed to be Deputy Director, contributing her knowledge and experience to the task of creating the new Division.

Dr. Sieber left DCEG in 1997 to serve as the Acting Director of the NCI Division of Cancer Control and Population Sciences, then moved to the NCI Office of the Director, where she eventually headed the new NCI Office of Communication.

She chaired the Etiology Working Group of the National Action Plan on Breast Cancer and served on the Board of Directors of the Reproductive Toxicology Center, the editorial board of the journal *Reproductive Toxicology,* and the U.S. Army Breast Cancer Research Program Integration Panel. Additionally, she founded and chaired the NIH Inter-Agency Working Group on Breast and Gynecologic Cancer, chaired one of NCI's Institutional Review Boards, and headed the NCI Animal Care and Use Committee. She served on the faculty of the NIH Graduate Program and was chairperson of its Pharmacology and Toxicology Department.


Dr. Susan Sieber

Dr. Sieber enjoyed tackling challenging, controversial issues. During her tenure, she helped formulate the Institute's approach to the use of animals in laboratory research, human subjects protection, ethics and confidentiality concerns, women's health, environmental cancer, interagency coordination, communication and advocacy concerns, and a great many other matters. She contributed an enormous amount to NCI, and she will be greatly missed.