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DCEG Linkage

Division of Cancer Epidemiology and Genetics

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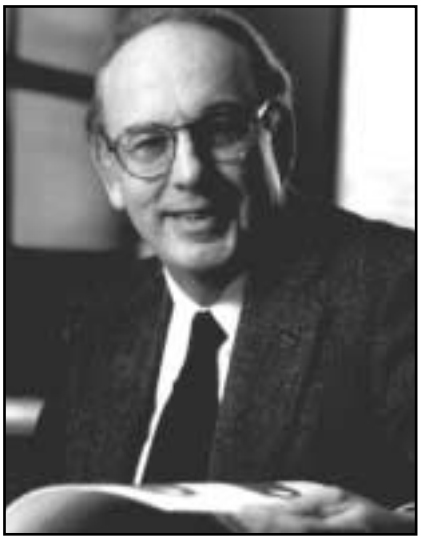
DIRECTOR'S PAGE

The Gene versus Environment Debate



Dr. Joseph F. Fraumeni, Jr.

Controversy has erupted in the wake of a recent study published in the *New England Journal of Medicine* (2000;343:78-85) that attempted to gauge the relative impact of genetic constitution and environmental exposure in the causation of cancer. In a large-scale survey of nearly 45,000 pairs of twins in Scandinavia, researchers estimated the contribution of inherited and environmental factors by comparing the risk of cancers arising in identical twins (who have the same set of genes) versus fraternal twins (who share about 50 percent of their genes). Among the major forms of cancer, estimates of the genetic component ranged from 27 percent for breast cancer to 42 percent for prostate cancer; the remaining percentages for each tumor were assumed to be attributable to lifestyle and other environmental exposures.

Although the estimates of heritability in the twin study were greater than those previously derived from family-based surveys of cancer, a blizzard of press accounts emphasized that inherited genes play only a limited role in the causation of cancer, in contrast to lifestyle and other environmental exposures. Because the twin study was published soon after the announcement that scientists were rapidly nearing complete deciphering of the human genome, the media raised concerns that the attention devoted to the Human Genome Project and to the study of cancer-associated genes might be misplaced.

The study of twins has long been a useful approach for distinguishing the relative importance of inherited and environmental factors in disease, but the statistical methods employed by the Scandinavian investigators assumed that genes and environment were acting in isolation, rather than in combination. In a thoughtful editorial entitled "Cancer—nature, nurture, or both," Dr. Robert Hoover, Director of DCEG's Epidemiology and Biostatistics Program, discussed the limitations of the twin study and the conclusions that should be drawn from the results (*N Engl J Med* 2000;343:135-136).

In this article, Dr. Hoover noted that the epidemiologic patterns of various cancers reflect to a large extent the impact of environmental exposures (e.g., tobacco, alcohol,

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dietary factors, radiation, infectious agents, and environmental chemicals), but mounting evidence indicates that one's genetic makeup influences susceptibility or even resistance to cancer-causing exposures. It is well known, for example, that not all elderly men who smoked heavily most of their lives develop lung or other tobacco-related cancers. Why? By integrating new genetic technologies into epidemiologic research, not only will it be possible to identify the genes that modify one's risk of developing cancer, but the resulting insights into genetic pathways should help uncover previously unsuspected exposures that may cause cancer. This approach has been outlined in a recent DCEG paper (Rothman N, Wacholder S, Caporaso N, Garcia-Closas M, Buetow K, Fraumeni JF Jr. The use of common genetic polymorphisms to enhance the epidemiologic study of environmental carcinogens. *Biochim Biophys Acta Rev Cancer* 2000;1471(2):C1-C10 [published online August 10]).

In assessing the overall impact of genes in the development of cancer, it is important to consider the role played by acquired as well as inborn genetic alterations. It is thus essential to understand how environmental carcinogens disrupt genes in the target tissue to cause cancer, and to identify and characterize the gene mutations that underlie the initiation and proliferation of cancer cells. The challenge for DCEG and NCI is to identify the cascade of inherited and somatic mutations associated with the origins and progression of cancer and to apply this knowledge to better define cancer risk and to devise new diagnostic, preventive, and even therapeutic strategies. The dichotomy suggested by the gene versus environment debate actually serves to downplay the potential contribution of both factors by neglecting the impact of their interactions. Yet it is this dynamic interplay between genes and environment that may account for a large proportion of human cancer, multiply the opportunities for preventive interventions, and hold the key to its eventual control. ■

Joseph F. Fraumeni, Jr., M.D.

THE CHORNOBYL THYROID PROJECT

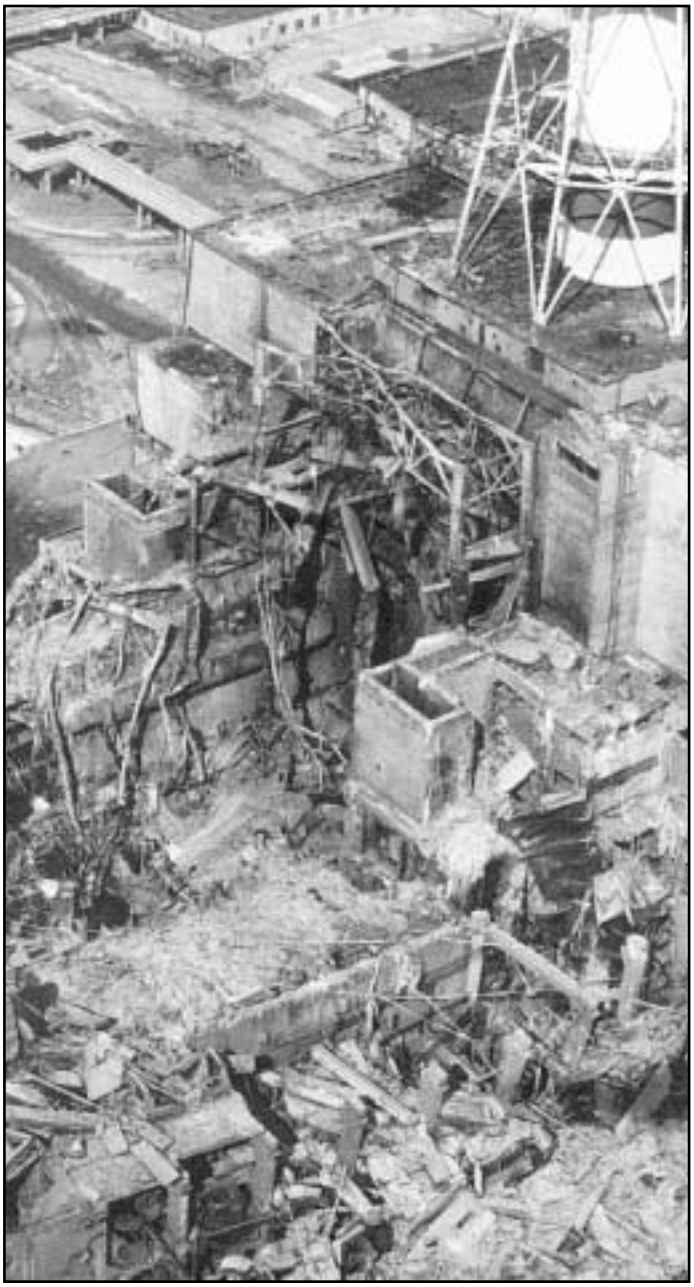
In April 1986, an explosion rocked Unit 4 of the Chornobyl Nuclear Power Plant in what is now Ukraine. Thousands of people were exposed to radiation, including unborn babies, children, and the cleanup workers sent to contain the damage.

NCI has been studying the effects of the Chornobyl explosion since the early 1990's, when the U.S. Department of Energy (DOE) invited NCI to develop protocols that could assess the health effects of the accident. Dr. Bruce Wachholz, then Chief of the Division of Cancer Biology's Radiation Effects Branch, managed the scientific aspects of the program for nearly a decade. In early 1999, the research program was transferred to DCEG and solidified into the Chornobyl Research Unit (CRU), which now consists of seven NCI staff members and is headed by Dr. Gilbert Beebe.

The CRU's research program includes two projects. One, a study of the accident's effects on thyroid neoplasia in persons exposed to the radiation as children in Ukraine and Belarus, has been under way for several years. The other, a study of leukemia prevalence among cleanup workers in Ukraine, is in the pilot phase. Program funding totaled $1.8 million in fiscal year 1998 and $3.1 million in fiscal year 1999. NCI, DOE, and the U.S. Nuclear Regulatory Commission contribute funds.

DCEG set up a Chornobyl Oversight Panel, chaired by Dr. Shelia Zahm, which meets monthly to review the program and recommend changes to strengthen its epidemiology and execution. An external peer review group has been established for the thyroid study. In addition, a Binational Advisory Group exists for both the Ukraine and the Belarus components of the thyroid study; each Group consists of five U.S. scientists and five scientists from the country.

The thyroid project aims to screen 12,000 residents, in each country, who were less than 19 years old at the time of the explosion and had measurements of thyroid radioactivity within 2 months of the accident. Scientists screen residents, compare earlier thyroid measures with more recent ones, and reconstruct the radiation dose for each person with the help of residential and dietary information and other environmental measurements. Ideally, each person will be reexamined every 2 years for the next 15 to 20 years.



Chornobyl Unit 4

In Ukraine, approximately 11,000 persons have been screened at least once; in Belarus, 9,400 people have been screened at least once. The CRU

researchers plan to publish a paper on the history, methodologies, and protocols of the thyroid study by the end of 2001. Also by then, a draft paper describing the prevalence of thyroid abnormalities in each country should be completed. NCI plans to merge the Ukraine and Belarus studies into one.

The Columbia University School of Public Health provides valuable scientific and technical collaboration for the thyroid project. The principal investigator is Dr. Geoffrey Howe, professor of epidemiology at the School of Public Health. Dr. Ihor Masnyk serves as project officer for the Columbia contract. Other agencies involved in the research program include DOE, the ministry of health and other governmental agencies in Ukraine and Belarus, the U.S. Nuclear Regulatory Commission, the U.S. Environmental Protection Agency, and France's Institute for Protection and Nuclear Safety.

In November 1999, the NCI sponsored the first trinational meeting on the Chornobyl thyroid project. A second meeting on November 13–15, 2000, involved participants from the United States, Ukraine, and Belarus in an in-depth discussion of study progress and future plans.

Researchers with the thyroid project are doing more than just collecting data. Unsuspected thyroid cancer has been detected in both countries, and other thyroid complications have also been identified. The project is building awareness of the problem among the Ukrainian and Belarusian populations and educating people on the need for screening and early detection and treatment of thyroid abnormalities. In addition, Ukraine and Belarus are benefiting from technology transfer, including ultrasound and computer technologies. ■

Nancy Volkers

BREAST IMPLANTS AND BREAST CANCER

An estimated 1.5 million to 2.0 million U.S. women have had breast implant surgery since 1962. The safety of breast implants has been questioned, in the popular press and in the courtroom, since the first reports in the mid-1980's that women with these implants developed connective tissue diseases and other disorders. Originally, the implants were assumed to be biologically inactive and therefore safe.

In 1992, the U.S. Food and Drug Administration decided to limit the availability of the implants to women who were undergoing breast reconstruction in controlled clinical trials, until the long-term safety of the implants for all women could be established. In addition, Congress charged NIH with conducting a follow-up study to study the health effects of the implants. In response, DCEG investigators initiated a large-scale study to assess whether silicone breast implants altered the risk of breast cancer, other cancers, and various connective tissue diseases, such as rheumatoid arthritis, Sjögren's syndrome, and scleroderma.

Dr. Louise Brinton, Chief of the Environmental Epidemiology Branch, and colleagues have reported results of the first stage of the analysis in the November issue of *Cancer Causes and Control* (2000;11:819-827). "This is the largest study with the longest follow-up to date, and we don't see an alteration in the risk of breast cancer for patients with breast implants," Dr. Brinton said. "The women in this study were followed for more than 10 years, and their risk is the same as women in the general population."

Dr. Louise Brinton

Dr. Brinton's results stand in contrast to many previous reports that women with breast implants have a lower risk of breast cancer than women in the general population. Those studies typically followed fewer women for less than 10 years. In addition, "The reduction in breast cancer found in those shorter studies may just be reflecting the intensive screening that women considering implants get prior to their surgery," Dr. Brinton said. "Earlier studies may be reflecting a pre-screening bias. Cases were diagnosed 'early,' creating a larger-than-expected rate of breast cancer during the study's observation period. But in one study, this result did not occur. We found that over the long run, the breast cancer risk appears to be the same as other women."

The DCEG study looked at 13,500 women who received cosmetic breast implants in both breasts between 1962 and 1989. The researchers compared these women to 4,000 women of a similar age with plastic surgery of a different sort, such as face-lifts and tummy tucks. The researchers selected women from 18 plastic surgery practices in six geographic areas: Atlanta, Birmingham, Charlotte, Miami, Orlando, and Washington, DC. Following assurance of patient confidentiality, physicians from these practices agreed to give DCEG investigators access to patients' medical records.

The DCEG researchers reviewed the records of these women and mailed questionnaires asking about their health status. Women with any type of breast implant—silicone gel filled, saline filled, or double lumen (double sac implants with silicone gel in the inner sac and saline in the outer sac)—were studied. None of the implants affected the risk of breast cancer. Although women with implants who developed breast cancer tended to have their cancer detected at slightly later stages than women without implants, breast cancer mortality did not differ significantly between the two groups of women.

Nevertheless, "One of the concerns with the implants is that cancers won't be discovered until they become more advanced," Dr. Brinton said. "We may not have enough precision at the moment to resolve the issue. That's why it's very important to continue to follow these patients to see if the breast cancer death rates change over time."

In addition to continuing to follow breast cancer in these patients, the researchers are continuing to study these women to evaluate the risk of other cancers and connective tissue disorders, as well as causes of death. ■

Lisa Seachrist

DIAGNOSTIC X-RAYS AND BREAST CANCER

Studies of atomic bomb survivors, tuberculosis patients, and patients irradiated for other medical conditions have established that exposure to ionizing

Ms. Michele Doody

radiation, especially during childhood and adolescence, increases the risk of breast cancer in adulthood. But the exact magnitude of risk for repeated small doses of radiation that cumulate over a period of time remains unclear. In the August 15 issue of *Spine* (2000;25:2052-2063), epidemiologist Michele Doody of the Radiation Epidemiology Branch and colleagues have reported that women who received repeated, small x-ray doses as scoliosis patients in the 1960's have a greater risk of dying from breast cancer than women in the general population.

Ms. Doody and colleagues built upon a small pilot study, conducted in the mid-1980's, that showed a nearly twofold risk of incident breast cancer among scoliosis patients. They studied 5,466 women with scoliosis who received on average 24.7 x-rays. These women had been diagnosed with scoliosis at a young age (less than 19 years) and before 1965, when radiation doses for x-rays were higher than they are today. Their treatment involved routine diagnostic x-rays during the growth spurt to monitor the progression of spine curvature and the effectiveness of treatment.

"This is a very interesting population," Ms. Doody said. "It's one of few groups where we have young women exposed to repeated low doses of radiation during childhood and adolescence, who've then been followed for 40 to 50 years into adulthood. We are very interested in exposures that occurred during breast budding and menarche, a period when the breasts might be particularly sensitive to the carcinogenic action of radiation."

The researchers focused their initial analysis on mortality. They found that women who had been diagnosed with scoliosis as children were 70 percent more likely to die from breast cancer than were women in the general population.

The risk of dying from breast cancer increased significantly as the cumulative number and dosage of x-rays increased. Patients who had 50 or more x-ray exams were four times more likely to die from breast

cancer than women in the general population, and women who had received a dose of 20 centigrays were more than three times more likely to die from breast cancer. The study found no persuasive evidence that risk differed according to age at exposure within narrow age ranges during the adolescent period.

According to Ms. Doody, "This study provides more evidence that radiation exposure, especially at young ages, is associated with increased breast cancer risk later in life." The findings from this study confirm the importance of reducing radiation exposures to the extent possible without adversely affecting the quality of care of the patient. Physicians should be aware that patients treated for scoliosis many years ago may be at increased risk for breast cancer.

As Ms. Doody points out, persons with scoliosis shouldn't avoid treatment out of fear of developing breast cancer. "We want to be very careful not to discourage people with scoliosis from receiving appropriate treatment since, if left untreated, this disease can be very debilitating," Ms. Doody said. "It's important to note that today's exposures are much lower than exposures during the time period covered by this study, and breast cancer risks related to today's exposures are presumably much lower."

The study is far from over. Ms. Doody and her colleagues have recently begun to evaluate the incidence of breast cancer related to repeated low-dose radiation exposures, and this time they are taking into account other risk factors, such as parity, age at first birth, and use of exogenous estrogens. "Based on questionnaire responses from more 3,100 patients, it appears that those with the most severe scoliosis received the largest radiation doses and were also the least likely to have had children," said Ms. Doody. "Since being childless is a risk factor for developing breast cancer, it is possible that some of the observed excess in breast cancer mortality could be related to reproductive history."

The researchers indicated that continued follow-up of these patients (average age, 51 years) is warranted since they are just now entering the ages when breast cancer occurs naturally. With the identification of additional cases, risk estimates can be better defined and the errors in the risk estimates reduced. ■

Lisa Seachrist

SENIOR STATISTICIAN SPENDS SABBATICAL AT DCEG

Dr. Joseph Gastwirth

Last year, Dr. Joseph Gastwirth took time away from his post as a professor of statistics and economics at George Washington University to serve as a visiting scientist at DCEG. His career has touched on a wide variety of topics, ranging from discrimination practices to genetics, and he has taken his love and understanding of statistics to the courtroom and the scientific arena with equal facility. Dr. Gastwirth recently authored the book *Statistical Science in the Courtroom* (see page 21).

DCEG Linkage caught up with Dr. Gastwirth to see how his year at DCEG went.

How did you first become interested in statistics?

If my mother were still alive she would tell you that she knew I'd end up doing something with numbers because as a child, I would make her read the number at the bottom of the page in the book she was reading me. Seriously, I was always very good with numbers, and I don't think there was ever any doubt that I would do something quantitative.

Why do you think you've been able to touch on so many disciplines in your career?

First of all, statistical methods tend to be far broader in application than people think. Many issues that arise in health arise also in economics and sociology.

What types of issues?

For example, when I was working as a statistical consultant for the Office of Management and Budget (OMB), I was asked if I'd had any experience analyzing several 2 x 2 tables or the Mantel-Haenszel test and the related estimator of the common odds ratio in all the tables. OMB wanted to review a U.S. Food and Drug Administration proposal to warn the

public of the link between Reye syndrome and prior use of aspirin to alleviate symptoms of flu or chicken pox in children.

Incidentally, a procedure used to analyze matched case-control data that was developed by Dr. Mitchell Gail and Dr. Jay Lubin of DCEG was also an important tool in the OMB data analysis. The method allows statisticians to examine case-control data for evidence of causation of disease. That same method was also useful in examining hiring and promotion data for evidence of possible discrimination. There really is a lot of similarity in observational data.

How do you choose which projects you want to attack?

I try to look at problems that are applicable across several different areas. It makes life more interesting. The difficulty is that I think everything is interesting.

What were some of the projects you worked on while at DCEG?

One project concerned using pooled samples to identify genetic mutations. This method dates back to World War II, when pooled blood analysis was used to test for venereal disease in groups of soldiers. They would test a batch of blood from 10 soldiers. Most of the time the batch was negative, saving money. Samples from individuals in the batches that tested positive were tested to identify carriers. Also, to estimate prevalence one can simply use the results of the tests of the group of 10, which enables one to preserve the privacy of individuals as well. Drs. Joni Rutter, Ruth Pfeiffer, Mitchell Gail, and I explored whether the method is applicable to identify mutation carriers or estimate the prevalence of a mutation in the population.

We found one can pool samples from five to nine individuals and still identify whether the pool has a *BRCA1* or *BRCA2* mutation. Currently, we are extending these ideas to estimate the joint prevalence of alleles at different loci. Again we hope to examine the privacy issues associated with genetic studies to see whether grouping methods may be useful in assuring participants that they won't be identified.

A less involved project concerned the applicability of latent class models in assessing the comparative accuracy of three screening tests for human herpesvirus 8, for which there is no gold standard test. Collaborating with Dr. Eric Engels, others from the Viral Epidemiology Branch, and a former Ph.D. student of mine, Dr. Michael Sinclair, we were able to determine the best test. The paper will appear soon in the *International Journal of Cancer*.

Dr. Nilanjan Chatterjee, of the Biostatistics Branch, was working with Dr. Ellen Velie, a postdoc, on the relationship between dietary fat intake and breast cancer. Because of the skewness of the data, the usual method of summarizing data in terms of quartiles or quintiles was not very informative. I suggested looking at the full risk percentile curve. For example, a person at the 27th percentile may well have a risk closer to the members of the first quartile than the second quartile.

Along with Dr. Chatterjee and Dr. Barry Graubard, I am developing this idea further. We have obtained very interesting data from Dr. Regina Ziegler and Dr. Stephanie Weinstein on homocysteine levels and cancer. An advantage of the full risk percentile curve is that the attributable risk corresponds to an area between the curve and a baseline risk.

What were some of the most intellectually stimulating aspects of your time with DCEG?

I enjoyed talking with the postdoctoral and predoctoral students. They had some very interesting ideas.

Would you encourage today's statisticians to work in such diverse disciplines?

Recent Ph.D.'s have to specialize very early to make a name for themselves. They are under so much pressure to publish these days. If one is going to change research areas, it requires a lot of reading. I think that nowadays most people don't have the time to devote to it.

What was the most enjoyable aspect of your time spent at DCEG?

The opportunity to work on a variety of interesting problems and to find that some previous statistical methods I developed were applicable to a new

field—genetic epidemiology. In particular, Dr. Boris Freidlin and I applied a method for obtaining robust tests in nonparametric survival analysis and contingency tables to obtain procedures to analyze identical-by-descent-sharing data from affected sib-pairs data. The article will appear in the *Annals of Human Genetics*. Conversations with members of the Biostatistics Branch, as well as with Dr. Lynn Goldin, from the Genetic Epidemiology Branch, were quite helpful. Dr. Fraumeni and the other senior staff at DCEG provided a very encouraging atmosphere for research. This was the nicest aspect of my time at DCEG. ■

Lisa Seachrist

NCI AWARDS RECIPIENTS

Several members of the DCEG staff were honored at the 2000 NCI Awards Ceremony, which was held on September 27 in the Masur Auditorium. Congratulations to all the recipients for their exceptional achievements during the past year.

Length of Service Citation

Ihor Masnyk, Ph.D., in recognition of 40 years of service.

Dr. Ihor Masnyk

NIH Merit Awards

Barry Graubard, Ph.D., for extraordinary efforts in developing a conceptual framework and evaluation design for the American Stop Smoking Intervention Study (ASSIST).

Allan Hildesheim, Ph.D., in recognition of international leadership in the epidemiologic study of host responses to human papillomavirus infections.

Dr. Allan Hildesheim

Debra T. Silverman, Sc.D., for important scientific contributions to our understanding of the causes of pancreatic cancer.

Dr. Debra T. Silverman

Mary Ward, Ph.D., for the creative use of geographic information systems to evaluate environmental exposure to pesticides.

PHS Citation

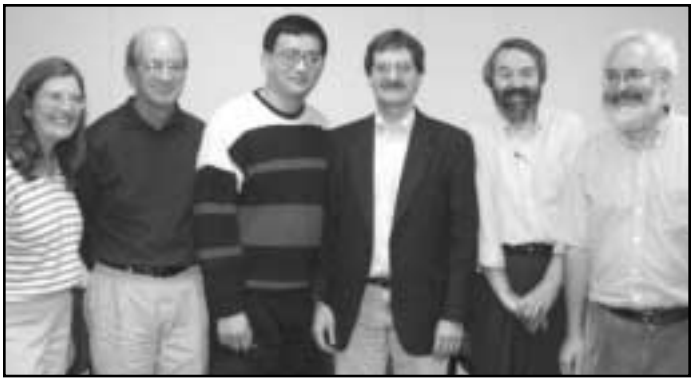
Mark Schiffman, M.D., for advancing the field of molecular epidemiology through efforts to improve communication across disciplines and to ensure access to high-quality laboratory approaches. ■

EVERYTHING YOU WANTED TO KNOW ABOUT MOLECULAR EPIDEMIOLOGY AND … NOW YOU CAN ASK

This fall, DCEG offered its first course in molecular epidemiology, which is designed to provide a practical perspective as well as a theoretical framework for molecular epidemiology studies. Dr. Nat Rothman, one of two Course Directors, hopes "to quickly integrate DCEG staff into ongoing studies and get them planning new projects, including methods and analytic studies, with a primary goal being to develop proposals for various funding mechanism within DCEG." He and Dr. Jim Vaught, the other Course Director, gathered a team of DCEG investigators to help design and lead the course. Team members include Drs. Ken Buetow, Neil Caporaso, Montserrat Garcia-Closas, Richard Hayes, Charles Rabkin, Mark Schiffman, Rashmi Sinha, and Sholom Wacholder. Ms. Kris Kiser, from the DCEG Office of Education, serves as Course Coordinator. Speakers include researchers from DCEG, NIH, and the local academic community.

Originally, the organizers thought the course would be attended by only recently arrived DCEG fellows and staff scientists. The interest, however, was overwhelming. Over 30 students, ranging from predoctoral fellows to senior investigators, are participating in the course. According to Dr. Schiffman, director of the new Molecular Epidemiology Fellowship Program, "The large attendance demonstrates that molecular epidemiology is now a predominant theme of the Division. The fellows from both laboratory and epidemiology backgrounds quite clearly see the need for fusion. While the faculty talks about moving increasingly toward interdisciplinary science, the students will embody it as the only kind of work some of them do."

Faculty and students confirm Dr. Rothman's characterization that this was "molecular epidemiology boot camp." Within a 3-month period, there are 34 hours of class time, 10 hours of lab site visits, and assigned readings from articles



Some recent contributors to the Molecular Epidemiology Course, left to right: Ms. Kris Kiser, Dr. Jim Vaught, Dr. Xia Xu, Dr. Paul Strickland, Dr. Terry Phillips, Dr. Nat Rothman

and the two course texts: *Application of Biomarkers in Cancer Epidemiology* (IARC Scientific Pub #142) and *Metabolic Polymorphisms and Susceptibility to Cancer* (IARC Scientific Pub #148). Students are required to prepare and present proposals for a methodologic study by the middle of the course and an analytic study at the end. Course topics include a theoretical framework for using biologic markers in cancer epidemiology; sources of funding within DCEG; study design; quality control; molecular, physical, and biochemical methods of analysis; data analysis; and manuscript preparation. Terms such as HPLC, GS/MS, RIA, ELISA, real-time PCR, and MALDI-TOF are no longer "Greek" to the non-laboratory course participants. Students also learn about logistical issues of developing protocols, collecting and shipping samples, laboratory processing, storing samples in a biorepository, and the BSI II system (a biospecimen management database). Researchers give case reports on a variety of biomarkers used in genetic, infectious disease, nutritional, and toxicological studies.

Dr. Vaught has organized tours of a biorepository, the Laboratory of Population Genetics (LPG) Advanced Technology Center, and a molecular pathology lab to expose students to the practicalities of managing a molecular epidemiology study. Dr. Vaught observed that, "Over the years, DCEG investigators have learned many valuable lessons through problems they have encountered in collecting, processing, shipping, and storing specimens. I think the discussions of methodologic issues in class and the

visit to the biorepository have given the students a good appreciation of the complexities and costs of handling large numbers of specimens. Several students have expressed an interest in following up on ideas to improve on our specimen processing methods."

Some course participants also taught portions of the course. Dr. Xia Xu, a fellow in the Environmental Epidemiology Branch (EEB), discussed the analytical methods he employed for his study of endogenous estrogen metabolism. Ms. Patti Gravitt, another EEB fellow, gave a talk with Dr. Schiffman on molecular analytic methods, focusing on nucleic acid hybridization and polymerase chain reaction. Dr. Joni Rutter, an LPG fellow, discussed a state-of-the-art method for genotyping using mass spectrometry.

A midcourse survey has confirmed that the course is demanding, but that students are enthusiastic about its future payoff. Dr. Yan Ban, a postdoctoral fellow in the Genetic Epidemiology Branch, remarked, "I think the idea of having this course is great. I have learned a lot from all the presenters. It is particularly helpful to me because I have a molecular epidemiology project going on now. Perfect timing." Dr. Aleyamma Mathew, a visiting scientist in the Nutritional Epidemiology Branch (NEB), said, "This course is quite useful for me to plan and conduct a collaborative pilot study between NEB and the Regional Cancer Center, Trivandrum, Kerala, India. For this study we will collect biological samples and assess various biomarkers." Dr. Juan Alguacil, a fellow in the Occupational Epidemiology Branch, commented, "The faculty has helped us put the acquired knowledge into practice by requiring two study proposals. While developing our study proposals, we received feedback not only from the rest of students but also from the faculty members during the presentation sessions."

Dr. Hayes commended the course directors. "Nat Rothman and Jim Vaught have done a great job of organizing this course for beginning investigators in molecular epidemiology," he said. "Easily as useful as the course content is the opportunity for students to interact in a very practical way with other scientists on topics of mutual interest." ■

DCEG SUMMER FELLOWS

The DCEG Summer Research Program, which is committed to supporting student interns interested in exploring careers in cancer epidemiology and genetics, is open to high school, college, and graduate students. Successful applicants join the Division for at least 8 weeks between June and August and, under supervision, conduct research in selected areas of epidemiologic or laboratory investigation. Students also attend lectures in the Summer Seminar Series, participate in DCEG meetings and seminars, attend formal NIH lectures and symposia, and participate in the Summer Research Program Poster Day.

Dr. Joseph Fraumeni with DCEG summer student interns

For the summer of 2000, competition for summer positions was steep. DCEG received over 150 applications and hired 12 students. Three of the interns presented their projects at the NIH Summer Poster Session held on the NIH campus. Afterward they displayed their posters at Executive Plaza South and fielded questions from dozens of DCEG investigators.

Many thanks to the students' dedicated mentors: Ms. Joanne Colt, Ms. Marianne Henderson, and

Drs. Andrew Flood, Mark Greene, James Goedert, Allan Hildesheim, Katherine McGlynn, Charles Rabkin, Carl Schaefer, Mark Schiffman, Jim Vaught, Sholom Wacholder, Mary Ward, Stephanie Weinstein, and Regina Ziegler, all of DCEG, and Dr. Diane Solomon of the Division of Cancer Prevention.

Recruitment will begin in January 2001 for next summer. Students interested in applying to this program should send a cover letter indicating interests relevant to the Division's research mission, along with a curriculum vitae, to Ms. Kris Kiser, Office of Education, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Executive Plaza South, MSC 7242, Bethesda, MD 20892, e-mail: ncidceg-r@mail.nih.gov. ■

DCEG RECIPIENTS OF FELLOWS AWARD FOR RESEARCH EXCELLENCE 2001

Four DCEG fellows received an NIH Fellows Award for Research Excellence (FARE) 2001, which recognizes intramural postdoctoral fellows for their outstanding research. The winners receive a $1,000 travel award that can be used to present their work at a scientific meeting. FARE awardees also participate in poster presentations accompanying the NIH Wednesday Afternoon Lecture Series, and they become judges for FARE 2002.

Below are the DCEG fellows who were honored at a ceremony on October 31 in Wilson Hall, and the titles of their winning abstracts. Congratulations!

Nilanjan Chatterjee, Biostatistics Branch, "Association and aggregation analysis using kin-cohort designs with applications to genotype and family history data from the Washington Ashkenazi Study."

Michael Hauptman, Biostatistics Branch, "Statistical methods for the investigation of effects of timing of exposure in epidemiologic studies and their application to asbestos exposure and lung cancer."

David Kaufman, Laboratory of Population Genetics, "Segregation analysis of 236 families of breast cancer cases without *BRCA1/2* mutations provides statistical evidence of a major recessive breast cancer susceptibility gene with high penetrance."

James Lacey, Environmental Epidemiology Branch, "Ovarian cancer risk associated with estrogen replacement therapy and estrogen-progestin replacement therapy in a prospective cohort study." ■

FELLOWS TOWN MEETING WITH DR. FRAUMENI

The Committee of Scientists (COS) hosted a DCEG fellows town meeting with Division Director Dr. Joseph F. Fraumeni, Jr., on September 21. Before the meeting, Dr. Jim Lacey and Dr. Andrew Flood, the COS members who moderated the meeting, surveyed DCEG fellows about issues they wished to have addressed by Dr. Fraumeni. Dr. Shelia Zahm and Dr. Trisha Hartge also attended and provided their insights.

The meeting began with a discussion of the research directions of DCEG. Dr. Fraumeni reviewed the recently published National Academy of Sciences report *Enhancing the Postdoctoral Experience for Scientists and Engineers*, which includes a list of 10 action points for improving the quality of postdoctoral life. Dr. Zahm presented data that demonstrated a diverse range of qualifications and accomplishments of the DCEG investigators recently appointed to tenure-track positions. Dr. Hartge noted several high-profile projects in which fellows played a significant role in shaping DCEG research priorities. The meeting then moved to a discussion of what fellows should expect from and seek in DCEG mentors. The meeting concluded with a discussion of career advancement issues: promotion requirements, obtaining short-term training in long-term epidemiologic studies, and allocating time to multiple concurrent projects.

RECENT SCIENTIFIC HIGHLIGHTS

Bladder Cancer

Cigarette Smoking and Bladder Cancer Risk

A meta-analysis of data from 16 bladder cancer studies conducted in the general population (n = 1,999 cases) revealed an interaction between smoking and *N*-acetyltransferase 2 slow acetylation (odds ratio = 1.3). Assuming a 2.5-fold elevation in bladder cancer risk from smoking, the estimated attributable risk among persons who had ever smoked was 35 percent for slow acetylators and 13 percent for rapid acetylators. (Marcus PM, Hayes RB, Vineis P, Garcia-Closas M, Caporaso NE, Autrup H, Branch RA, Brockmoller J, Ishizaki T, Karakaya AE, Ladero JM, Mommsen S, Okkels H, Romkes M, Roots I, Rothman N. Cigarette smoking, *N*-acetyltransferase 2 acetylation status, and bladder cancer risk: A case-series meta-analysis of a gene-environment interaction. *Cancer Epidemiol Biomarkers Prev* 2000;9:461-467) ■

Breast Cancer

Dietary Fat and Breast Cancer among Postmenopausal Women

Over 40,000 postmenopausal women who had participated in a national breast cancer mammography screening program and completed a food-frequency questionnaire were followed for an average of 5.3 years; 996 of these women developed breast cancer. Compared with that for women in the lowest quintile of percentage of energy from total fat, the adjusted risk ratio for women in the highest quintile was 1.1. A positive association was observed among women with no history of benign breast disease (risk ratio = 2.2). The increased risk appeared because of intake of unsaturated fat, particularly oleic acid. (Velie E, Kulldorff M, Schairer C, Block G, Albanes D, Schatzkin A. Dietary fat, fat subtypes, and breast cancer in postmenopausal women: A prospective cohort study. *J Natl Cancer Inst* 2000;92:833-839)

Menstrual Risk Factors and Early-onset Breast Cancer

Menstrual cycle characteristics, such as early menarche, rapid initiation of regular ovulatory cycles, short cycle length, and more days of flow, were assessed in relation to breast cancer in women under age 45. Compared with women with menarche at age 15 or older, an increased risk of breast cancer was observed in women with earlier menarche. Women who reported regular menstrual cycles within 2 years of menarche were at increased risk relative to those who never had regular cycles. Slightly stronger associations with menstrual characteristics were observed among thinner women than heavier women. (Butler LM, Potischman NA, Newman B, Millikan RC, Brogan D, Gammon MD, Swanson CA, Brinton LA. Menstrual risk factors and early-onset breast cancer. *Cancer Causes Control* 2000;11:451-458) ■

Colon Cancer

Eating Frequency and Risk of Colon Cancer

Case-control studies have found elevated risk of colorectal cancer with higher eating frequency. This analysis used information collected prospectively from the Epidemiologic Follow-Up Study of the First National Health and Nutrition Examination Survey. The study population of 9,978 subjects followed from 1982–1984 to 1992 yielded 141 colorectal cancer cases. Compared with persons eating less than 3 times a day, those eating 3 to 4 times a day had a relative risk for colorectal cancer of 0.66, but those eating more than 4 times a day had a relative risk of 0.7. The decreased risk was associated with more meals, rather than more snacks, per day. (Tseng M, Ingram DD, Darden R, Ziegler RG, Longnecker MP. Eating frequency and risk of colorectal cancer. *Nutr Cancer* 2000;36:170-176)

Iron Levels and Recurrence of Colon Adenoma

This study assessed whether serum ferritin concentration was associated with recurrence of colorectal adenomas among 733 persons from a multicenter clinical trial with baseline determinations

of ferritin. Risk of adenoma recurrence increased modestly among participants with a ferritin concentration higher than 70 g/L relative to those with lower ferritin (odds ratio = 1.4). Dietary intake of iron and red meat was inversely associated with adenoma recurrence among participants with replete iron stores, but not consistently associated among those with nonreplete stores. (Tseng M, Greenberg ER, Sandler RS, Baron JA, Haile RW, Blumberg BS, McGlynn KA. Serum ferritin concentration and recurrence of colorectal adenoma. *Cancer Epidemiol Biomarkers Prev* 2000;9:625-630) ■

Genetics

Quantifying Bias Due to Population Stratification in Epidemiologic Studies

Data on the frequency of the *N*-acetyltransferase slow acetylation genotype and incidence rates of male bladder cancer and female breast cancer in non-Hispanic U.S. Caucasians with ancestors from eight European countries were used to assess the potential bias in risk estimate resulting from population stratification. Theoretical calculations showed that ignoring ethnicity leads to a bias of 1 percent or less. Furthermore, evaluation of a wide range of allele frequencies and representative ranges of cancer rates that exist across European populations showed a bias of less than 10 percent in U.S. studies, except under extreme conditions. Also, the bias decreased as the number of ethnic strata increased. (Wacholder S, Rothman N, Caporaso N. Population stratification in epidemiologic studies of common genetic variants and cancer: Quantification of bias. *J Natl Cancer Inst* 2000;92:1151-1158)

p53 Splice Site Mutations in Three Li-Fraumeni Families

Germline mutations in the p53 tumor suppressor gene predispose persons to a variety of cancers in families with Li-Fraumeni syndrome. Most germline *p53* mutations observed to date cause amino acid substitutions in the protein's central sequence-specific DNA-binding domain. However, this study found novel alterations outside this conserved core region, in sequences that regulate precursor mRNA splicing, in three Li-Fraumeni syndrome families. Two splice site mutations affected the consensus sequence at the splice donor sites of introns 1 and 9 and produced unstable variant transcripts in normal cells. A third mutation at the splice acceptor site of intron 9 generated splicing at a cryptic acceptor site in intron 9. These splice site alterations emphasize the need to examine both noncoding and untranslated regions of the *p53* gene for germline mutations in Li-Fraumeni syndrome families. (Verselis SJ, Rheinwald JG, Fraumeni JF Jr, Li FP. Novel p53 splice site mutations in three families with Li-Fraumeni syndrome. *Oncogene* 2000;19:4230-4235)

Characterization of Ataxia Telangiectasia Mutations

In this collaborative study, 41 families with ataxia telangiectasia from Denmark, Finland, Norway, and Sweden were screened for ataxia telangiectasia mutations. The protein truncation test, fragment length, and heteroduplex analyses of large cDNA fragments (0.8 to 1.2 kb) were used. In total, 67 of 82 disease-causing alleles were characterized. Thirty-seven unique mutations were detected, of which 25 have not previously been reported. One-third of the probands (13) were homozygous, whereas the rest (26) were compound heterozygotes with at least one identified allele. (Laake K, Jansen L, Hahnemann JM, Brondum-Nielsen K, Lonnqvist T, Kaariainen H, Sankila R, Lahdesmaki A, Hammarstrom L, Yuen J, Tretli S, Heiberg A, Olsen JH, Tucker M, Kleinerman R, Borresen-Dale AL. Characterization of ATM mutations in 41 nordic families with ataxia telangiectasia. *Hum Mutat* 2000;16:232-246) ■

Kidney Cancer

Obesity, Hypertension, and the Risk of Kidney Cancer in Men

The incidence of kidney cancer was evaluated among 363,992 Swedish men who underwent at least one physical examination from 1971 to 1992 and were followed until death or the end of 1995. Men with

renal cell cancer (n = 759) and renal pelvis cancer (n = 136) were identified by cross-linkage of data with the nationwide Swedish Cancer Registry. Compared with men in the lowest three eighths of the cohort for body mass index, men in the middle three eighths had a 30 to 60 percent greater risk of renal cell cancer, and men in the highest two eighths had nearly double the risk. There was also a direct association between higher blood pressure and a higher risk of renal cell cancer. The risk was substantially higher in men after exclusion after 5 years of follow-up. At the sixth year of follow-up, the risk rose further with increasing blood pressure and decreased with decreasing blood pressure, after adjustment for baseline measurements. Men who were current or former smokers had a greater risk of both renal cell cancer and renal pelvis cancer than men who were not smokers. There was no relation between body mass index or blood pressure and the risk of renal pelvis cancer. (Chow WH, Gridley G, Fraumeni JF, Jarvholm B. Obesity, hypertension, and the risk of kidney cancer in men. *N Engl J Med* 2000;343:1305-1311) ■

Leukemia

Leukemia following Treatment for Testicular Cancer

A study of 36 leukemia cases and 106 controls was undertaken within a cohort of 18,567 patients who were diagnosed with testicular cancer from 1970 through 1993. Radiotherapy (mean dose to active bone marrow, 12.6 Gy) without chemotherapy was associated with a threefold elevated risk of leukemia. The estimated relative risk of leukemia at a cumulative dose of 650 mg cisplatin, commonly administered in current treatment regimens, was 3.2; larger doses (1,000 mg) were linked with sixfold increased risks. Nonsignificant excesses were estimated for current radiotherapy regimens limited to the abdomen and pelvis. Among 1,000 patients given a treatment dose of 25 Gy and followed for 15 years, an excess of nine leukemias was predicted; cisplatin-based chemotherapy (dose, 650 mg) might result in 16 cases of leukemia. (Travis LB, Andersson M, Gospodarowicz M, van Leeuwen FE, Bergfeldt K, Lynch CF, Curtis RE, Kohler BA, Wiklund T, Storm H, Holowaty E, Hall P, Pukkala E, Sleijfer DT, Clarke EA, Boice JD, Stovall M, Gilbert E. Treatment-associated leukemia following testicular cancer. *J Natl Cancer Inst* 2000;92: 1165-1171) ■

Lung Cancer

Lung Cancer and Environmental Tobacco Smoke

A population-based case-control study of lung cancer and environmental tobacco smoke (ETS) among persons who had never smoked was conducted in two rural prefectures of China. There were 200 female and 33 male lung cancer cases, and 407 female and 114 male controls. The odds ratio (OR) for ever exposed to ETS was 1.2, with a significant trend with increasing exposure. ORs were 1.0, 1.0, 1.1, and 1.5 for nonexposed, exposed less than 10 pack-years, exposed 10 to 19 pack-years, and exposed 20 or more pack-years, respectively. Excess risks were limited to ETS exposures in childhood (OR = 1.5), with a significant trend for increasing pack-years of childhood exposure (OR = 1.0, 1.4, 1.8, and 3.0, respectively). (Wang L, Lubin JH, Zhang SR, Metayer C, Xia Y, Brenner A, Shang B, Wang Z, Kleinerman RA. Lung cancer and environmental tobacco smoke in a non-industrial area of China. *Int J Cancer* 2000;88:139-145)

Dietary Heterocyclic Amines and Risk of Lung Cancer

A population-based study of 593 cases and 623 frequency-matched controls was conducted among Missouri women to investigate lung cancer risk posed by different heterocyclic amines (HCAs) in the diet. When comparing the 90th and 10th percentiles, researchers observed significant excess risks for consumption of MeIQx (odds ratio [OR] = 1.5), but not for DiMeIQx (OR = 1.2) or PhIP (OR = 0.9). MeIQx consumption was associated with increased risk of lung cancer for nonsmokers (OR = 3.6) and light/moderate smokers (OR = 2.1), but not for heavy smokers (OR = 1.0). Risk was increased with MeIQx intake for squamous cell carcinomas (OR = 1.9) and "other" histologic types (OR = 1.6), but not for small-cell carcinomas or

adenocarcinomas. Neither DiMeIQx nor PhIP showed an association with smoking categories or lung cancer histology. (Sinha R, Kulldorff M, Swanson CA, Curtin J, Brownson RC, Alavanja MC. Dietary heterocyclic amines and the risk of lung cancer among Missouri women. *Cancer Res* 2000;60:3753-3756)

Indoor Coal Combustion Emissions, GSTM1 and GSTT1 Genotypes, and Lung Cancer Risk

This collaborative study analyzed glutathione *S*-transferase mu 1 (GSTM1) and theta 1 (GSTT1) genotypes in a population-based case-control study of 122 lung cancer cases and 122 controls in Xuan Wei County, an area of China with high lung cancer risk and indoor use of smoky coal. Compared with subjects who used less than 130 tons of smoky coal during their lifetime, heavier users had an increased risk of lung cancer (odds ratio = 2.4). The GSTM1-null genotype was also associated with increased risk (odds ratio = 2.3). Smoky coal use appeared to be strongly associated with lung cancer risk among GSTM1-null versus GSTM1-positive individuals. In contrast, the GSTT1 genotype was not significantly associated with lung cancer risk. (Lan Q, He X, Costa DJ, Tian L, Rothman N, Hu G, Mumford JL. Indoor coal combustion emissions, GSTM1 and GSTT1 genotypes, and lung cancer risk: A case-control study in Xuan Wei, China. *Cancer Epidemiol Biomarkers Prev* 2000;9:605-608) ■

Lymphoma

Incidence Patterns of Non-Hodgkin's Lymphoma by Histology

Clinical investigations have shown prognostic heterogeneity for the non-Hodgkin's lymphomas (NHL) according to histology. This study used data collected by the Surveillance, Epidemiology, and End Results study to assess the demographic patterns and increases in population-based rates of different histologic subgroups of NHL. Among the 60,057 NHL cases diagnosed during 1978–1995, total incidence (per 100,000 person-years) was 17.1 among white males, 11.5 among white females, 12.6 among black males, and 7.4 among black females. Rates for follicular NHL were two to three times greater among whites than blacks, with little variation by sex. Blacks had a much higher incidence than whites for peripheral T-cell NHL, and incidence was higher among males than females. High-grade NHL was the most rapidly rising subtype, particularly among males. Follicular NHL increased more rapidly among black males than in the other racial or gender groups. (Groves FD, Linet MS, Travis LB, Devesa SS. Cancer surveillance series: Non-Hodgkin's lymphoma incidence by histologic subtype in the United States from 1978 through 1995. *J Natl Cancer Inst* 2000;92:1240-1251)

Second Cancers among Survivors of Pediatric Hodgkin's Disease

This study analyzed data from 5,925 children with Hodgkin's disease (HD), including 2,646 10-year and 755 20-year survivors, who were reported to 16 population-based cancer registries in North America and Europe between 1935 and 1994. A total of 157 solid tumors (observed / expected ratio [O / E] = 7.0) and 26 acute leukemias (O / E = 27.4) were reported. At 20 years, risk of solid tumors persisted (O / E = 6.6); even at 25 years, risk remained high (O / E = 4.6). Greater than 50-fold increased risks were observed for tumors of the thyroid and respiratory tract among children treated before age 10. After HD diagnosis at older ages (10 to 16 years), the largest number of second cancers occurred in the digestive tract (O / E = 19.3) and breast (O / E = 22.9). Relative, but not absolute, risks of solid tumors increased with decreasing age at HD diagnosis. These results underscore the importance of lifelong follow-up of pediatric HD patients who had been aggressively treated. (Metayer C, Lynch CF, Clarke EA, Glimelius B, Storm H, Pukkala E, Joensuu T, van Leeuwen FE, van't Veer MB, Curtis RE, Holowaty EJ, Andersson M, Wiklund T, Gospodarowicz M, Travis LB. Second cancers among long-term survivors of Hodgkin's disease diagnosed in childhood and adolescence. *J Clin Oncol* 2000;18:2435-2443) ■

Malignant Melanoma

Changing Patterns of Melanoma

From 1950–1954 through 1990–1994, melanoma mortality rates increased in the United States by 191 percent among U.S. white males and 84 percent among white females. Mortality rates peaked in the 1930–1950 birth cohorts for females and in the 1935–1950 birth cohorts for males. In the 1950–1969 study period, melanoma mortality rates followed a strong north-south gradient, which weakened in more recent periods. The absolute change in mortality for a 10 percent increase in ultraviolet B among females decreased from 0.08 additional deaths per 100,000 person-years in 1950–1959 to 0.01 additional deaths in 1990–1995. In contrast, the absolute change in mortality among males showed little change over time. The changing patterns reflect the interplay of ultraviolet radiation levels, sun-protection behaviors, population mobility, risk awareness, and early detection practices. (Jemal A, Devesa SS, Fears TR, Hartge P. Cancer surveillance series: Changing patterns of cutaneous malignant melanoma mortality rates among whites in the United States. *J Natl Cancer Inst* 2000;92:811-818)

Clinical Features in Malignant Melanoma Families with Different Gene Mutations

Two genes have been implicated by DCEG studies in the development of cutaneous malignant melanoma (CMM). *CDKN2A* is a tumor suppressor gene that encodes p16. Germline mutations of *CDKN2A* have been detected in 10 to 25 percent of melanoma-prone families, some of whom are also prone to pancreatic cancer. *CDK4* is a protooncogene. Germline mutations in this gene were found in only three melanoma-prone families to date. This study compared 104 CMM case subjects from 17 CDKN2A families and 12 CMM case subjects from 2 CDK4 families. The median age at CMM diagnosis and the median numbers of CMMs did not differ between CDKN2A and CDK4 families. Assessment of CMM case subjects from CDKN2A families with and without pancreatic cancer revealed no significant differences in median age at diagnosis or in tumor number. There was, however, a significant difference in age-adjusted median numbers of nevi; CMM case subjects from CDKN2A families without pancreatic cancer had greater numbers of nevi. Clinical factors were otherwise indistinguishable between CDKN2A and CDK4 families. (Goldstein AM, Struewing JP, Chidambaram A, Fraser MC, Tucker MA. Genotype-phenotype relationships in U.S. melanoma-prone families with CDKN2A and CDK4 mutations. *J Natl Cancer Inst* 2000;92:1006-1010)

Dysplastic Nevi and the CDKN2A Gene in Melanoma Families

A combined segregation / linkage analysis was used to examine the relationship between CDKN2A and dysplastic nevi (DN), total nevi, and solar injury. Genetic and covariate data were collected on 20 American melanoma-prone families, 13 of which had cosegregating *CDKN2A* mutations. Overall, the likelihood score improved when DN, total nevi, or both covariates were added to the base model, which included dominant transmission of the *CDKN2A* gene and a linear increase of risk with the logarithm of age on the logit scale. Inclusion of solar injury did not significantly improve the likelihood for the base model. Significant evidence for a gene-covariate interaction was detected between DN and CDKN2A when DN was the only covariate in the model, or when both DN and total nevi were in the model. In both methods, the odds ratio for DN was greater in subjects without (20.1) than in those with *CDKN2A* mutations (3.3). (Goldstein AM, Martinez M, Tucker MA, Demenais F. Gene-covariate interaction between dysplastic nevi and the CDKN2A gene in American melanoma-prone families. *Cancer Epidemiol Biomarkers Prev* 2000;9:889-894) ■

Methodologic Studies

The Effects of Timing of Exposure on Disease Risk

This study presents an exploratory method to analyze the effects of timing of exposure on disease risk in epidemiologic studies when exposure histories are available. The method includes the fitting of a

series of risk models, each including different parts of the exposure histories. The differences in the goodness-of-fit and the parameter estimates among the fitted models provide insight into effects of timing of exposure. A recent German lung cancer case-control study indicated that the number of cigarettes smoked 2 to 11 years before disease onset is most predictive of lung cancer risk. Among smokers with the same cumulative number of cigarettes, those with a greater number of cigarettes smoked within 20 years before interview had greater lung cancer risk. (Hauptmann M, Lubin JH, Rosenberg PS, Wellmann J, Kreienbrock L. The use of sliding time windows for the exploratory analysis of temporal effects of smoking histories on lung cancer. *Stat Med* 2000;19:2185-2194)

Reproducibility and Concordance for Female Plasma Androgen Assays

This study determined the magnitude and sources of variability in androgen assay results and tried to identify laboratories capable of performing such assays for large epidemiologic studies. A single sample of plasma was obtained from five postmenopausal women, five premenopausal women in the midfollicular phase of the menstrual cycle, and five premenopausal women in the midluteal phase. Results suggest that a single sample of androstanediol glucuronide, dehydroepiandrosterone, dehydroepiandrosterone sulfate, and androsterone glucuronide (two lab replicates per sample) can be used to reliably discriminate among women in a given menstrual phase or menopausal status. The results for dihydrotestosterone, testosterone, androstenedione, and androsterone sulfate are less reliable, so present measurement techniques should be used with care, especially with women in the midluteal phase. The results for androstanediol suggest that this assay is not yet ready for use in epidemiologic studies. (Fears TR, Ziegler RG, Donaldson JL, Falk RT, Hoover RN, Stanczyk FZ, Vaught JB, Gail MH. Reproducibility studies and interlaboratory concordance for androgen assays in female plasma. *Cancer Epidemiol Biomarkers Prev* 2000;9:403-412)

A New Method of Collecting Buccal Cell DNA

An evaluation of Guthrie cards, which were pretreated to retard bacterial growth and inhibit nuclease activity, found that the cards provide a simple, noninvasive, cost-effective alternative to brushes/swabs and mouth rinses for collecting buccal cell DNA for molecular epidemiology studies. Five days after the oral mucosa was brushed and the mouth fluid was collected onto a card, 90 percent of the samples were amplified in all three β-globin gene fragment assays. Although samples stored up to 9 months at -70ºC had reduced DNA yields, they were still successfully amplified. (Harty LC, Garcia-Closas M, Rothman N, Reid YA, Tucker MA, Hartge P. Collection of buccal cell DNA using treated cards. *Cancer Epidemiol Biomarkers Prev* 2000;9:501-506) ■

Multiple Myeloma

Socioeconomic Status and Multiple Myeloma in Blacks and Whites

This population-based case-control study examined the relation between socioeconomic status (SES) and the risk of multiple myeloma among blacks and whites in three areas of the United States. Inverse gradients in risk were associated with occupation-based SES, income, and education. Risks were significantly elevated for subjects in the lowest categories of occupation-based SES (odds ratio [OR] = 1.7), education (OR = 1.4), and income (OR = 1.4). Occupation-based low SES accounted for 37 percent of multiple myeloma in blacks and 17 percent in whites, as well as 49 percent of the excess incidence in blacks. Low education and low income accounted for 17 and 28 percent of the excess incidence in blacks, respectively. SES-related factors thus account for a substantial amount of the black-white differential in multiple myeloma incidence. (Baris D, Brown LM, Silverman DT, Hayes R, Hoover RN, Swanson GM, Dosemeci M, Schwartz AG, Liff JM, Schoenberg JB, Pottern LM, Lubin J, Greenberg RS, Fraumeni JF Jr. Socioeconomic status and multiple myeloma among US blacks and whites. *Am J Public Health* 2000;90:1277-1281) ■

Nasopharyngeal Cancer

Nitrosamines and Nasopharyngeal Cancer

In a case-control study conducted in Taiwan, researchers interviewed 375 nasopharyngeal carcinoma (NPC) patients and 327 controls about their diet as adults and at age 10, using a food-frequency questionnaire. Mothers of the participants were interviewed about their child's diet, during weaning and at ages 3 and 10, and about their own diet while breastfeeding. Intake of nitrosamines and nitrite as an adult was not associated with risk of NPC, but high intake of nitrosamines and nitrite during weaning and childhood, for foods other than soy products, was associated with increased risk of NPC. The adjusted odds ratio for the highest quartile was 3.9 for weaning, 2.6 for age 3, and 2.2 for age 10. Intake of nitrite and nitrosamines from soybean products during childhood and weaning was inversely associated with risk. (Ward MH, Pan WH, Cheng YJ, Li FH, Brinton LA, Chen CJ, Hsu MM, Chen IH, Levine PH, Yang CS, Hildesheim A. Dietary exposure to nitrite and nitrosamines and risk of nasopharyngeal carcinoma in Taiwan. *Int J Cancer* 2000;86:603-609) ■

Prostate Cancer

CAG Repeat Lengths in the AR Gene and Prostate Cancer Risk

A population-based case-control study in China investigated whether CAG repeats and other polymorphisms of the *AR* gene are associated with clinically significant prostate cancer in this low-risk population. Genomic DNA from 190 prostate cancer patients and 304 healthy controls was sequenced to evaluate the relationship between CAG and GGN (polyglycine) repeat length and prostate cancer. Compared with western men, study subjects had a longer CAG repeat length. The median was 23 repeats, and only 10 percent of the subjects had a CAG repeat length shorter than 20. Compared with men with a longer CAG repeat length, men with a CAG repeat length shorter than 23 had a 65 percent increased risk of prostate cancer. This study indicates that Chinese men have a longer CAG repeat length than western men and that even in a very low-risk population, a shorter CAG repeat length confers a higher risk of clinically significant prostate cancer. (Hsing AW, Gao Y-T, Wu G, Wang X, Deng J, Chen Y-L, Sesterhenn IA, Mostofi FK, Benichou J, Chang C. Polymorphic CAG and GGN repeat lengths in the androgen receptor gene and prostate cancer risk: A population-based case-control study in China. *Cancer Res* 2000;60:5111-5116)

Lifestyle and Anthropometric Risk Factors for Prostate Cancer

Cancer-free control patients who participated in a population-based case-control study from 1986 through 1989 (81 percent response rate) were followed through 1995 for cancer incidence by their linkage to the Iowa Cancer Registry; 101 incident prostate cancers were identified. After data adjustment for age, family history of prostate cancer, body mass index, total energy, and intake of meat, men who consumed less than 22 g alcohol / week (RR = 1.1), 22 to 96 g alcohol / week (RR = 2.6), and more than 96 g alcohol / week (RR = 3.1) were at increased risk of prostate cancer compared with nonusers of alcohol. Body mass index was weakly and positively associated with prostate cancer after the data were adjusted for age, but this association strengthened after multivariate adjustment and exclusion of well-differentiated localized tumors. (Putnam SD, Cerhan JR, Parker AS, Bianchi GD, Wallace RB, Cantor KP, Lynch CF. Lifestyle and anthropometric risk factors for prostate cancer in a cohort of Iowa men. *Ann Epidemiol* 2000;10:361-369)

Male Pattern Baldness and Prostate Cancer

Male pattern baldness (MPB) and prostate cancer are common in American males; however, MPB is clinically observable decades earlier. Aging, androgens, and heritability are risk factors for both

conditions. This prospective study—the Epidemiologic Follow-Up Study of the First National Health and Nutrition Examination Survey—examined the association between MPB and clinical prostate cancer in a cohort representative of the U.S. male population. The age-standardized incidence of prostate cancer was greater among men with baldness at baseline (17.5 versus 12.5 per 10,000 person-years). The adjusted relative risk for prostate cancer among men with baldness was about 1.5, regardless of the severity of baldness at baseline and independent of other risk factors, including race and age. (Hawk E, Breslow RA, Graubard BI. Male pattern baldness and clinical prostate cancer in the epidemiologic follow-up of the first National Health and Nutrition Examination Survey. *Cancer Epidemiol Biomarkers Prev* 2000;9:523-527) ■

Stomach Cancer

Gastric Dysplasia and Gastric Cancer

A follow-up study was launched in 1989–1990 among 3,433 adults in Linqu County, China, to determine the risk factors for progression of precancerous gastric lesions in this high-incidence area. The presence of *Helicobacter pylori* at baseline was associated with an increased risk of progression to dysplasia or gastric cancer (odds ratio = 1.8) during the 4.5-year follow-up. The risk of progression also was increased with the number of years of smoking cigarettes and with the number of cigarettes smoked. In contrast, the risk of progression was decreased by 80 percent (odds ratio = 0.2) among subjects with baseline ascorbic acid levels in the highest (compared with the lowest) tertile. Risk was not affected by the serum level of retinol, β-carotene, selenium, or ferritin or by the zinc-to-copper ratio. (You WC, Zhang L, Gail MH, Chang YS, Li J, Jin ML, Hu YR, Yang CS, Blaser MJ, Correa P, Blot WJ, Fraumeni JF Jr, Xu GW. Gastric dysplasia and gastric cancer: *Helicobactor pylori*, serum vitamin C, cigarette smoking, and other risk factors. *J Natl Cancer Inst* 2000;92:1607-1612) ■

Viruses

Cancer Risk in Children with AIDS

Among 4,954 children with AIDS, 124 were identified as having cancer diagnosed between 1978 and 1996 before, at, or after AIDS onset. This number included 100 cases of non-Hodgkin's lymphoma (NHL), 8 of Kaposi's sarcoma, 4 of leiomyosarcoma, 2 of Hodgkin's disease, and 10 other or unspecified cancers. In the first 2 years after AIDS diagnosis (5,485 person-years), NHL incidence was 510 per 100,000 person-years (relative risk [RR] = 651). The most common type of NHL was Burkitt's lymphoma, but the risk of primary brain lymphoma (91 per 100,000 person-years) was especially high (RR = 7,143). Leiomyosarcomas tended to occur several years after AIDS onset, with three of the four cases occurring 33 to 76 months after AIDS diagnosis. In contrast, Kaposi's sarcoma was reported usually within 2 years of AIDS diagnosis. Risk of Hodgkin's disease risk was also significantly increased (RR = 62). The spectrum of AIDS-associated pediatric cancers resembled that seen in adults, with the addition of leiomyosarcoma. (Biggar RJ, Frisch M, Goedert JJ. Risk of cancer in children with AIDS. *JAMA* 2000;284:205-209)

Effect of Hepatitis G Virus Infection on Progression of HIV Infection in Hemophilia Patients

In a study of 131 patients from comprehensive hemophilia treatment centers in the United States and Europe who became HIV positive between 1978 and 1985, 60 patients who were positive for hepatitis G virus (HGV) had higher CD4+ lymphocyte counts and 12-year AIDS-free survival rates (68 percent) compared with HGV-negative patients (40 percent), despite similar ages and HIV viral loads. Risk for AIDS was 40 percent lower for HGV-positive patients independent of age, HIV and hepatitis C viral loads, CD4+ and CD8+ lymphocyte counts, and CCR5 genotype. (Yeo AE, Matsumoto A, Hisada M, Shih JW, Alter HJ, Goedert JJ. Effect of hepatitis G virus infection on progression of HIV infection in patients with hemophilia: Multicenter Hemophilia Cohort Study. *Ann Intern Med* 2000;132:959-963)

Identifying Human Herpesvirus 8 Infection

Sensitivity and specificity were evaluated on four enzyme-linked immunoassays and one immunofluorescence assay for human herpesvirus 8 (HHV-8). All performed reasonably well in distinguishing between infected and uninfected persons for use in most epidemiologic studies. A classification tree was developed in terms of seropositivity. (Engels EA, Whitby D, Goebel PB, Stossel A, Waters D, Pintus A, Contu L, Biggar RJ, Goedert JJ. Identifying human herpesvirus 8 infection: Performance characteristics of serologic assays. *J Acquir Immune Defic Syndr* 2000;23:346-354)

HTLV-I-associated Myelopathy or Tropical Spastic Paraparesis

Human T-cell lymphotropic virus type I (HTLV-I) is associated with adult T-cell leukemia/lymphoma and a chronic neurologic disease called HTLV-I-associated myelopathy or tropical spastic paraparesis (HAM/TSP). The potential mechanisms of HAM/TSP pathogenesis were assessed by examination of two pathways initiated by interferon-γ, a predominant cytokine in HAM/TSP. In Jamaican HAM/TSP patients, significantly elevated levels of neopterin ($p = 0.003$) and kynurenine ($p = 0.05$) and a decreased level of tryptophan ($p = 0.003$) were found in the cerebrospinal fluid compared with patients with other neurologic diseases. These results suggest a role for immune activation within the central nervous system, particularly involving the indoleamine-2,3-dioxygenase pathway, in HAM/TSP. (Maloney EM, Morgan OSC, Widner B, Werner ER, Fuchs D. Central nervous system activation of the indoleamine-2,3-dioxygenase pathway in human T cell lymphotropic virus type I-associated myelopathy/tropical spastic paraparesis. *J Infect Dis* 2000;181:2037-2040)

Clinical and Biologic Correlates of HTLV-I-associated Infective Dermatitis

Infective dermatitis is the earliest disease manifestation of human T-cell lymphotropic virus type I (HTLV-I) infection in children and may be a harbinger of HTLV-I-associated diseases in adult life. Between January 1989 and August 1990, 212 HTLV-I-seropositive women who attended either of two antenatal clinics in Kingston, Jamaica, and their children were enrolled in a study of risk factors for maternal-to-child transmission. In a 10-year follow-up of 28 HTLV-I-infected children, 1 developed infective dermatitis, diagnosed at 46 months and 19 months following seroconversion. This child had a high HTLV-I proviral load at time of infection, similar to levels reported among adults with adult T-cell leukemia/lymphoma or with HTLV-I-associated myelopathy or tropical spastic paraparesis. The proviral load and antibody titer increased in a linear fashion over the course of follow-up. The ratio of CD4+ T-cells to CD8+ T-cells was elevated, as were activated T-cells, and remained so 2 years after diagnosis. The human leukocyte antigen class II haplotype revealed alleles consistent with the haplotype reported for other HTLV-I-associated diseases, suggesting that the susceptibility to these outcomes in infective dermatitis patients may be related to a shared immunogenic predisposition marked by human leukocyte antigen haplotypes. (Maloney EM, Hisada M, Palmer P, Brooks K, Pate E, Wiktor SZ, Lagrenade L, Manns A. Human T cell lymphotropic virus type I-associated infective dermatitis in Jamaica: A case report of clinical and biologic correlates. *Pediatr Infect Dis J* 2000;19:560-565) ■

BOOK ANNOUNCEMENTS

Statistics and the Law

Dr. Joseph Gastwirth, a Professor of Statistics and Economics at George Washington University who spent his 1999–2000 sabbatical year in the Biostatistics Branch, has edited a book, *Statistical Science in the Courtroom*. The book is a collection of articles written by statisticians and legal scholars concerned with problems arising from the use of statistical evidence in legal trials. Some articles describe DNA evidence and the difficulties of properly calculating the probability of a match between the evidence and a random person's profile, as well as the best way to interpret the result. Several authors tell about their experiences in court. Other articles describe the role of statistical evidence in cases concerning discrimination against minorities, product liability, environmental regulation, and the appropriateness and fairness of sentences. Still others address how being involved in legal statistics has raised interesting statistical problems that require further research. (Gastwirth JL, ed. *Statistical Science in the Courtroom*. New York: Springer-Verlag Press, 2000)

Statistics in Epidemiology

Dr. Mitchell Gail and Dr. Jacques Benichou have edited the *Encyclopedia of Epidemiologic Methods*, a single volume consisting of 180 revised and updated articles from *The Encyclopedia of Biostatistics* along with additional articles written by leading experts from academia, government, and industry exclusively for this publication. Intended for use by practitioners and researchers, the encyclopedia contains introductory articles on the epidemiology of genetics, infectious disease, nutrition, occupation, case-control and other epidemiologic designs, logistic regression and survival analysis, and cross-references to related topics. (Gail MH and Benichou J, eds. *Encyclopedia of Epidemiologic Methods*. Chichester, UK: Wiley Press, 2000)

PEOPLE IN THE NEWS

Dr. Michael Alavanja

Captain Michael Alavanja, a member of the Occupational Epidemiology Branch, received the 2000 Career Scientist Award at the PHS Commissioned Officers Association's annual meeting in June in Scottsdale, Arizona. This award recognizes a senior Commissioned Officer scientist who has made a sustained and superior contribution to biomedical science and public health through research and mentoring. Presented by the Surgeon General of the United States, the award cited Dr. Alavanja's work in lung cancer etiology, including key papers on environmental tobacco smoke and gene interactions, domestic radon exposure and monitoring methods, dietary factors, cooking practices, pre-existing nonmalignant disease, and family history of lung cancer. The award citation also recognized Dr. Alavanja's role as the principal investigator of the Agricultural Health Study, his work in developing a mentoring program for scientists within the PHS Commissoned Corps, his 2-year service as Chairperson of the PHS Professional Advisory Panel to the Surgeon General of the United States, and his work in initiating several new programs directed at career development of junior officers.

Captain Linda Brown, a member of the Biostatistics Branch, received her Dr.P.H. from the Uniformed Services University of the Health Sciences in May. One of her "hooders" at the graduation ceremony was **Dr. Terry Thomas**, now in the Radiation Epidemiology Branch, who was her thesis advisor. Dr. Brown completed degree requirements and wrote her dissertation, titled "*Helicobacter pylori* transmission and risk factors for infection in


Dr. Linda Brown

rural China," under a PHS Commissioned Corps long-term training grant. In addition, Dr. Brown was appointed PHS Board Chair of the Commissioned Officers Association in July. The Board Chair is the highest office of the organization, which has over 6,500 members.

Ms. Jerilyn Eiland, a member of the Clinical Genetics Branch, was given an On-the-Spot award in recognition of her assistance in facilitating the use of DCEG's new video conferencing system.

Dr. Eric Engels, a member of the Viral Epidemiology Branch, was appointed as a tenure-track investigator in July.

Dr. Ruthann Giusti, a Clinical Genetics Branch member, has been awarded $100,000 in NIH Clinical Center carryover funds for "Breast Imaging Studies in Women at High Genetic Risk of Breast Cancer." Awards were made based on innovation and potential to contribute to the clinical research revitalization efforts in the NIH intramural program. This project, the first of Clinical Genetics Branch's clinical studies, will start accruing participants early next year.

In August, **Dr. Barry Graubard**, a member of the Biostatistics Branch, was elected a fellow of the American Statistical Association at the annual meeting in Indianapolis.

Dr. Michie Hasada, a Viral Epidemiology Branch member, was appointed as a tenure-track investigator in August.


Dr. James Lacy

In July, **Dr. James Lacey**, a member of the Environmental Epidemiology Branch, won the first annual DCEG Fellowship Achievement Award.


Dr. Aparna Mohan

Dr. Aparna Mohan, a Radiation Epidemiology Branch fellow who is enrolled in the epidemiology doctoral program at the Johns Hopkins School of Hygiene and Public Health, recently won the prize for best student poster at the American College of Epidemiology Annual Scientific Meeting in Atlanta. Her poster was entitled "Mortality among radiologic technologists in the United States." **Ms. Ruth Kleinerman**, **Dr. Zhanat Abylkassimova**, and **Dr. Michal Freedman** of the Radiation Epidemiology Branch also attended the meeting and presented posters. In addition, **Dr. Martha Linet** led a roundtable discusson entitled "Scientific publication: the ongoing revolution." **Dr. Trisha Hartge** was the cochair of the program committee for the meeting.

Dr. Wei-Cheng You, a member of the Biostatistics Branch, was elected a fellow of the American College of Epidemiology in May. In addition, he received an Award of National Science and Technology from the People's Republic of China for the NCI-BICR collaborative study of precancerous gastric lesions. ■

MS. DONNA GELLERSON, NEW ADMINISTRATIVE RESOURCE CENTER MANAGER

Ms. Donna Gellerson

Ms. Donna Gellerson, DCEG's new Administrative Resource Center (ARC) manager, joined NIH in 1992 as a Budget Analyst for the Office of Research Services. She soon realized that she did not want to analyze spreadsheets all day, so she decided to move into the administrative field. However, Ms. Gellerson wanted to stay at NCI because cancer research had always been important to her, in part because many people in her family have been struck by the disease.

Ms. Gellerson has a great deal of experience in creating innovative solutions and in leading teams, which is serving her well in DCEG. She started her administrative career in the summer of 1993 as an Administrative Officer in the Division of Basic Sciences. Later, she moved to the Laboratory of Tumor Immunology and Biology for 2 years, and then became the Deputy ARC Manager for the Building 10 ARC for 2 years. Ms. Gellerson then moved to the Division of Cancer Treatment and Diagnosis, where she gained extramural experience working with Dr. Robert Wittes. In November 1999, Ms. Gellerson was asked to take over the leadership of the DCEG ARC, and she was selected for the permanent position in January 2000.

Working for DCEG is stimulating and challenging, according to Ms. Gellerson. The ARC members and the DCEG staff have been very welcoming, and she looks forward to a long and rewarding career with DCEG. She will continue to look for opportunities to improve customer service and streamline administrative processes, and she would like to see the ARC develop a strong and stable partnership with the scientific staff to ensure that we all are working toward the same goals. ■

Melanie Keller

NEW COURSE OFFERED BY THE RADIATION EPIDEMIOLOGY BRANCH IN 2001

Time: Wednesdays, 2:30–4:45 pm
January 10–May 16 (tentative)

Place: Executive Plaza North,
Conference Room J or H

Course Description: This course will present an overview of the field of radiation epidemiology, with a focus on radiation-induced cancer. Topics will include types of radiation, sources of population exposure, radiation measurement, basic radiobiology, radiation dosimetry, selected issues in study design and data analysis, case studies of a variety of radiation-exposed populations, susceptible subgroups, environmental and genetic determinants of susceptibility, principles of radiation risk assessment and risk communication, and areas for further research.

Contact: Peter D. Inskip, Radiation Epidemiology Branch, NCI
Executive Plaza South, Room 7052
Phone: (301) 496-6600
e-mail: inskippe@mail.nih.gov

ADMINISTRATIVE RESOURCE CENTER STAFF ASSIGNMENTS

Over the past 6 months, there have been several staff assignment changes in the Administrative Resource Center. In addition, Ms. Donna Gellerson has reorganized the Center, so that an Administrative Officer and a Comprehensive Administrative Assistant work with each branch. The new assignments are as follows.

Office or Branch	Adminstrative Officer or Comprehensive Administrator	Comprehensive Administrative Assistant
Office of the Director	Myra Thomas	Shereè Majette
Epidemiology and Biostatistics Program, Office of the Director	Melanie Keller	Linda Littlejohn
Biostatistics Branch	Denise Stoneman	Shereè Majette
Environmental Epidemiology Branch	Myra Thomas	Shereè Majette
Nutritional Epidemiology Branch	Melanie Keller	Shereè Majette
Occupational Epidemiology Branch	Denise Stoneman	Linda Littlejohn
Radiation Epidemiology Branch	Roberto Minutillo	Linda Littlejohn
Viral Epidemiology Branch	Charlotte Mercanti	Shereè Majette
Clinical Genetics Branch	Melanie Keller	Linda Littlejohn
Genetic Epidemiology Branch	Charlotte Mercanti	Shereè Majette
Laboratory of Population Genetics	Patrick Miller	None

NEWS FROM THE TRENCHES

Biostatistics Branch

In May, **Dr. Linda Brown** gave an invited talk entitled "The role of race/ethnicity in the epidemiology of esophageal cancer" at the annual meeting of the American Gastroenterological Association, which met in San Diego. Her talk was sponsored by the Committee for Under-represented Minorities.

Dr. Nilanjan Chatterjee and **Dr. Ruth Pfeiffer** attended a Biostatistics, Genetics, and Epidemiology Team (BGET) meeting in Toronto in mid-September. Dr. Chatterjee's presentation was on "Risk estimates for kin-cohort studies," and Dr. Pfeiffer spoke on "Inference for environmental effects based on family data, taking into account ascertainment and random genetic effects."

Dr. Susan Devesa attended a working session in Greece in June to produce a chapter for a projected book on the topic "Cancer on the threshold of the

millennium." This chapter will contain international incidence and mortality rates for individual cancers. Dr. Devesa persuaded her coauthors to modify their log scales for all the rates in order to achieve consistency and permit evaluation of time trends.

In June, **Dr. Jay Lubin** cochaired the American Statistical Association conference on the health effects of radiation exposures in Park City, Utah.

In October, **Dr. Sholom Wacholder** delivered an invited talk to the Department of Epidemiology at the University of North Carolina. His topic was "Design of epidemiologic studies—new challenges to old paradigms." ■

Clinical Genetics Branch

Dr. Blanche Alter was invited to speak at the 12th Annual International Fanconi's Anemia Scientific Symposium in Amsterdam in October.

In October, **Dr. Mark Greene** participated in the Wallace H. Clark Memorial Symposium on Melanoma in Philadelphia. His talk was entitled "Major melanoma susceptibility genes—update 2000." He was also invited to give the 16th Annual Ella T. Grasso Memorial Lecture at Yale University in November and spoke on hereditary ovarian cancer.

Ms. Jennifer Loud taught two educational sessions (A Genetics Primer for the Nurse Practitioner, and Cancer Genetics) in November at the National Conference of Nurse Practitioners in Washington, DC.

In September, **Ms. June Peters** was an invited speaker at the opening conference of the Women's Breast Health Program at the Harrington Cancer Center in Amarillo, Texas, and at the Mautner Project Healing Works Conference on Breast Cancer in Washington, DC. In November, she presented several posters on psychosocial issues related to genetic counseling and led a peer supervision group for genetic counselors at the National Society of Genetic Counselors held in Savannah, Georgia. ■

Environmental Epidemiology Branch

In August, **Dr. Louise Brinton** spoke on "Active and passive cigarette smoking and breast cancer risk" at the American Chemical Society National Meeting, held in Washington, DC. In October, she presented a talk entitled "Breast cancer epidemiology and prevention" at the 6th Annual Perspectives in Breast Cancer Meeting, also in Washington, DC.

In October, **Dr. Ann Hsing** participated in a workshop on "Emerging opportunities in prostate cancer epidemiology," sponsored by NCI and held in Washington, DC. In September, Dr. Hsing gave a talk entitled "Epidemiologic risk factors for prostate cancer" at the Prostate Cancer State of the Art Symposium held in Interlaken, Switzerland. In June, she participated in a meeting on Prostate Cancer in Minority Populations sponsored by NIH and Virginia Commonwealth University and held in Richmond, Virginia. The workshop participants made recommendations to the NIH Office for Research on Minority Health concerning future research. ■

Genetic Epidemiology Branch

At the June meeting of the Society for Epidemiologic Research in Seattle, **Dr. Yan Bai** presented two posters concerning the use of family history information in case-control studies. One described a new approach to incorporate family size without bias, and the other focused on the definition of family history and its effect on measuring environmental factors when family history is treated as a covariate. Also at this meeting, **Dr. Christina Bromley** presented a paper titled "Heterogeneity of risk for melanoma, pancreatic cancer, and digestive cancers: a melanoma case-control study."

In May, **Dr. Mary Lou McMaster** presented a poster about incidence and survival patterns for chordoma in the United States for 1973–1995 at the annual meeting of the American Society of Clinical Oncology in New Orleans.

Dr. Dilys Parry was one of three American investigators invited to Chester, England, to participate in a 2-day workshop in July on "Future directions in NF2 (neurofibromatosis 2) and vestibular schwannoma research." The workshop organizers were from tertiary care hospitals in Manchester that are major referral centers for patients with NF2. In October, Dr. Parry presented a poster on predictors of vestibular schwannoma growth in NF2 at the annual meeting of the American Society of Human Genetics in Philadelphia. Also at this meeting, **Dr. Elizabeth McNeil** and **Dr. Gladys Glenn** presented a poster concerning challenges of two rare genetic syndromes that have comorbid effects on the nervous system in a large kindred.

In May, **Dr. Margaret Tucker** gave a presentation about the epidemiology of melanoma at the American Association for Cancer Research meeting "Melanoma: Basic Biology and Immunological Approaches to Therapy" in Woodlands, Texas. Also in May, Dr. Tucker gave an invited presentation about cancer genetics and oncogenes in patient care at the Whitehead Institute for Biomedical Research meeting "Genes and Society: Impact of New Technologies on Law, Medicine, and Policy," held in Cambridge, Massachusetts. In June, Dr. Tucker presented the keynote address at the American Statistical Association meeting on the health effects of radiation exposures in Park City, Utah. The title of her talk was "Major cancer susceptibility genes and radiation: what do we know?" ■

Nutritional Epidemiology Branch

At the Society for Epidemiologic Research meeting in Seattle in June, **Dr. Andrew Flood** presented a poster on the association of fruits and vegetables with colorectal cancer risk in a prospective cohort of women. He also presented a poster entitled "The association of folate, methionine, and alcohol with colorectal cancer in a prospective study of women" at the NIH Research Festival in October.

Dr. Ulrike Peters presented a poster entitled "Vitamin D, calcium, and vitamin D receptor polymorphism in colorectal adenomas" at the NIH Research Festival in October.

Dr. Arthur Schatzkin gave a presentation in June called "The Polyp Prevention Trial: implications for nutrition and cancer research" at the Fred Hutchinson Cancer Center in Seattle. In September, Dr. Schatzkin presented "The NIH-AARP diet and health study: power to detect diet and cancer associations attenuated by measurement error" at the Fourth International Conference on Dietary Assessment Methods held in Tucson, Arizona. In October, he presented a talk entitled "Guilt by non-association: why the epidemiology of diet and cancer is so exasperating" at a Columbia University seminar in New York.

In September, **Dr. Rashmi Sinha** presented her work on measurements of exposures and intermediate products (metabolites, DNA adducts, etc.) at the meeting of the Biostatistics, Genetics, and Epidemiology Team of the Cooperative Family Registries for Breast and Colorectal Cancer Studies in Toronto. In November, Dr. Sinha participated in the Nutritional Epidemiology Retreat at the International Agency for Research on Cancer in Lyon to discuss the possibility of conducting dietary studies in India.

Dr. Stephanie Weinstein and **Dr. Ulrike Peters** participated in the American Association for Cancer Research's Pathobiology of Cancer Workshop in July in Keystone, Colorado. ■

Occupational Epidemiology Branch

At the Agricultural and Environmental Health in Central Europe meeting in Slovakia in September, **Dr. Michael Alavanja** presented a talk on the Agricultural Health Study and served on an expert panel to assess opportunities for epidemiologic research associated with agricultural exposures in Central Europe.

Dr. Aaron Blair and **Dr. Shelia Zahm** organized a symposium on "Measurement of low dose exposures and inferences about risk" at the annual meeting of the Society for Epidemiologic Research in June. Speakers were Drs. Jay Lubin, Jack Siemiatycki, and Paul Demers. In November, Dr. Blair was also a co-organizer with Dr. Steve Blair, Institute of Aerobic Research, of a conference on "Physical Activity and Cancer" held in Dallas. **Drs. Zahm, Robert Hoover**,

and **Louise Brinton** participated in the conference. Dr. Blair served on an EPA Scientific Advisory Panel meeting to evaluate the risk of cancer from exposure to the herbicide atrazine. He was re-elected to a second term on the Board of the American College of Epidemiology, and at the annual meeting in September, he presented a poster on reliability of pesticide reporting among farmers.

In October, **Dr. Joseph Coble** and **Ms. Joanne Colt** presented posters at the annual meeting of the International Society for Exposure Assessment in Monterey, California. Dr. Coble's poster was entitled "Occupational exposures among pesticide applicators in the Agricultural Health Study," and Ms. Colt's poster was "Pesticides, PAH, and PCB congeners in house dust from four sites."

In October, **Dr. Mustafa Dosemeci** and **Dr. Omur Elci** presented papers at the International Congress of Public Health conference in Istanbul, Turkey. Dr. Elci's paper was entitled "Occupations and the risk of laryngeal cancer in Turkey," and Dr. Dosemeci's was "Tobacco, alcohol use, and risks of bladder and renal cancer in Turkey." In September, at the Nordic Meeting of Agricultural Health and Safety held in Malmo, Sweden, Dr. Dosemeci presented "Quantitative assessment of exposure to pesticides in the retrospective Agricultural Health Study." In October, Dr. Dosemeci also gave seminars on "Silica, silicosis, and lung cancer in China" at George Washington University and on "Exposure assessment for epidemiologic studies" at the Karolinska Institute in Stockholm.

Ms. Claudine Samanic presented during the spotlight session of the Society for Epidemiologic Research meeting in June in Seattle, Washington. Her paper was entitled "Obesity and gastrointestinal cancer risk among white and black U.S. Veterans."

In September, **Dr. Debra Silverman** cochaired the Risk Session of the NCI Pancreatic Cancer Progress Review Group held in Chantilly, Virginia. The meeting summarized the state of the science of pancreatic cancer, identified barriers to the research, and recommended priorities for future study.

Several scientists from the Branch participated in the International Society for Environmental Epidemiology Meeting in Buffalo, New York, in August. **Dr. Mary Ward** spoke on drinking water nitrate and risk of adult glioma in Nebraska, and **Dr. Ken Cantor** presented a poster on chlorinated drinking water and risk of renal cell and pancreas cancers in Iowa. **Dr. Erin Bell** gave a talk on the relationships between agricultural pesticide applications and maternal residence and fetal death, and **Dr. Anneclaire De Roos** spoke on parental occupational exposures to electromagnetic fields and the risk of neuroblastoma in offspring. ■

Radiation Epidemiology Branch

In June at Niagara-on-the-Lake, Ontario, **Dr. Peter Inskip** presented a talk, "Radiation and thyroid carcinogenesis," at the 6th International Conference on Long-term Complications of Treatment of Children and Adolescents for Cancer.

Dr. Martha Linet spoke on "Environmental exposures and childhood cancer: an overview," at the Scientific Symposium on Environmental Contaminants Affecting Children. The symposium, held in October in Austin, Texas, was sponsored by the Children's Environmental Health Institute and the Texas Medical Association.

In October, **Drs. Elaine Ron**, **Charles Land**, and **Kiyohiko Mabuchi** attended the 12th International Thyroid Congress in Kyoto, Japan. Dr. Ron presented a highlighted poster, "Thyroid abnormalities associated with childhood I-131 exposure from atmospheric emissions," as well as two other posters. Dr. Land also presented a highlighted poster, "Thyroid disease prevalence and fallout exposure in Kazakstan." ■

PROSTATE CANCER WORKSHOP

The Division of Cancer Control and Population Sciences and DCEG held a workshop entitled "Emerging Opportunities in Prostate Cancer Epidemiology" on October 12–13 in Washington, DC. The meeting brought together leading epidemiologists, geneticists, molecular biologists, and pathologists to identify new approaches for understanding the environmental and genetic determinants of prostate cancer and, in particular, to focus on reasons for the marked ethnic differences in prostate cancer rates in the United States. Participants reviewed key areas of epidemiologic research, including gene mapping in multiple-case families, hormones, growth factors, other endogenous attributes, nutrition, physical activity, anthropometry, infectious agents, and agricultural factors. Recent insights on early pathologic progression and tumor marker development were presented. Workshop participants focused on the future and considered the design and infrastructure needs for molecular epidemiologic studies of prostate cancer, including the use of large-scale prospective and interventional studies and the exploitation of advances in high-throughput genomic and proteomic characterization. The workshop highlighted the need for interdisciplinary collaboration to facilitate understanding of the causes of this common cancer and the means of prevention. A meeting report is in preparation. ■

VISIT OF CHINESE DELEGATION ON HUMAN GENETIC RESOURCES ADMINISTRATION

For nearly 20 years, DCEG investigators have collaborated with researchers from many Chinese academic and governmental institutes on a variety of epidemiologic studies. On September 5, DCEG hosted a visit by a delegation from the Chinese Human Genetic Resources Administration (Drs. Wang Ren-Wu, Tian Ling, Zhu Yan-Miao, Li Yue, and Gu Ma-Lin), which oversees Chinese exports of blood and other DNA-containing specimens collected in international collaborative research projects. This visit provided a forum for informational exchange regarding the process of application for biospecimen exports from China and the scientific and ethical guidelines for conducting research at NIH. The delegation was particularly interested in the Shanghai women's cohort study, a project initiated by Drs. Wei Zheng and Xiao-Ou Shu at Vanderbilt University in collaboration with the Shanghai Cancer Institute (Drs. Fan Jin and Yu-Tang Gao) and NCI (Drs. Wong-Ho Chow and Nathaniel Rothman). The study has enrolled 75,000 women and collected blood and urine samples from 57,000 of them. Collection of buccal cell and urine samples is planned for the remainder of the cohort members. The delegation met with Drs. Joseph Fraumeni and Shelia Zahm and heard presentations by DCEG staff, including Drs. Jim Vaught and Kenneth Buetow. The delegation also met with Drs. Sharon Hrynkow and Allen Holt at the Fogarty International Center.

COMINGS … GOINGS

Dr. Juan Alguacil has joined the Occupational Epidemiology Branch as a visiting fellow. Dr. Alguacil, a physician, recently received his Ph.D. in epidemiology and public health from the Universitat Autonoma de Barcelona. Since 1995, he has been a research fellow in the Unit of Clinical and Molecular Epidemiology of Cancer at the Institut Municipal d'Investigacio Medical in Barcelona. His research has focused on the environmental and genetic aspects of pancreatic cancer. He also worked as an invited scientist at the Finnish Institute of Occupational Health in 1998. Dr. Alguacil is located in EPS/8091, and he can be reached at 594-7902.

Dr. Blanche Alter, an internationally recognized expert in Fanconi's anemia and other myelodysplastic syndromes that predispose to leukemia and solid tumors, has joined the Clinical Genetics Branch as a cancer expert. Dr. Alter was formerly Chief of Pediatric Hematology and Oncology at the University of Texas in Galveston. She recently received an M.P.H. from the Johns Hopkins School of Hygiene and Public Health. Dr. Alter is located in EPS/7020 and can be reached at 594-7642.

Dr. Erin Bell has joined the Occupational Epidemiology Branch as a Cancer Research Training Award postdoctoral fellow. She has a Ph.D. in epidemiology from the University of North Carolina and an M.S. in epidemiology and biostatistics from the University of Massachusetts at Amherst. Her doctoral dissertation focused on fetal death associated with exposure to pesticides. She is interested in the relation of occupational and environmental exposures to cancer risk, and she is working with Dr. Mary Ward and others on pesticide exposures. Dr. Bell is located in EPS/8091 and can be reached at 594-7485.

Ms. Stephanie Boyd has joined the Administrative Resource Center under NCI's stay-in-school program. Ms. Boyd is majoring in graphic design, with a minor in business, at the University of Maryland, Baltimore County. Ms. Boyd is located in EPS/8083 and can be reached at 594-7209.

Dr. Philip Castle has joined the Environmental Epidemiology Branch as a cancer prevention fellow in the Division of Cancer Prevention. Dr. Castle received his Ph.D. in biophysics from Johns Hopkins University in 1995 and his M.P.H. from the same institution in 2000. Between 1995 and 1999, he was employed as a postdoctoral fellow in the Laboratory of Cellular and Developmental Biology of NIDDK. He is working with Dr. Allan Hildesheim and Dr. Mark Schiffman on immunological and hormonal risk factors for human papillomavirus infection and cervical neoplasia. He is located in EPS/7082 and can be reached at 402-7482.

Dr. Anneclaire Jenice De Roos has joined the Occupational Epidemiology Branch as a postdoctoral fellow. She received her Ph.D. in epidemiology from the University of North Carolina, Chapel Hill, and she previously received an M.P.H. in epidemiology and biostatistics from the University of California at Berkeley. Her dissertation explored parental occupational exposures and the risk of neuroblastoma in offspring. She will be working with Dr. Michael Alavanja on the Agricultural Health Study and with others on a variety of research topics. She is located at EPS/8091 and can be reached at 594-7902.

Ms. Jaclyn Dozier has joined the Environmental Epidemiology Branch as an office automation assistant. She is a senior at the University of Maryland, majoring in anthropology with a minor in biology. She is located in EPS/7063 and can be reached at 496-1691.

Dr. Wen-Yi Huang has joined the Occupational Epidemiology Branch as a staff scientist. Dr. Huang received her Ph.D. and M.S. in epidemiology from the University of North Carolina at Chapel Hill. Her doctoral dissertation and master's research were dedicated to the understanding of gene-environment interactions in the etiology of breast cancer using various biological markers, including HER-2/neu, PRAD1, p53, and estrogen and progesterone receptors. She worked at Glaxo Wellcome Inc. before joining DCEG. Dr. Huang is working with Dr. Richard Hayes on the Prostate, Lung, Colorectal, and Ovarian Cancer study. She is located at EPS/8109 and can be reached at 435-4710.

Ms. Niloufar "Neely" Kazerouni has joined the Clinical Genetics Branch as a predoctoral fellow. Ms. Kazerouni is a doctoral student at the Uniformed Services University of the Health Sciences. She is located in EPS/7013 and can be reached at 594-7296.

Ms. Jennifer Loud has joined the Clinical Genetics Branch as a cancer genetics research nurse. Ms. Loud has a master's degree in advanced practice nursing, and for the past 6 years she has been an adult nurse practitioner with NCI's Medicine Branch. Ms. Loud is located in EPS/7019 and can be reached at 435-8062.

Dr. Volker Mai joined the Nutritional Epidemiology Branch as a cancer prevention fellow. Dr. Mai received a B.S. in biochemistry and a Ph.D. in microbiology from the University of Georgia. He completed his M.P.H. with a concentration in quantitative methods at the Harvard School of Public Health. His main interests are the effects of diet on human health and the role of the microbial flora in the gut on colon cancer. Dr. Mai is located in EPS/7039 and can be reached at 496-4378.

Ms. Giovanna (Shereè) Majette joined the DCEG Administrative Resource Center (ARC) in July as a comprehensive administrative assistant. Coming from the ARC in the Division of Cancer Prevention, Ms. Majette brings over 9 years of personnel management experience in the Federal government. She is located in EPS/8053 and can be reached at 594-7478.

Dr. Aleyamma Mathew joined the Nutritional Epidemiology Branch as a visiting fellow. She received a Ph.D. in epidemiology in Finland and a master's degree in statistics in India. Dr. Mathew is involved in assessing organochlorine levels in serum and breast adipose tissues among breast cancer patients in Kerala, India. She is working also with Dr. Rashmi Sinha on colorectal adenoma risk, with Dr. Wong-Ho Chow on esophageal and gastric cancer risk, and with Dr. Arthur Schatzkin and Dr. Sinha on a pilot study of diet and cancer in India. She is located in EPS/7034 and can be reached at 594-7297.

Dr. Jay Nuckols is serving as a consultant to the Occupational Epidemiology Branch in environmental exposure assessment. Dr. Nuckols received his Ph.D. in environmental engineering from the University of Kentucky and his M.S. in civil engineering from Northwestern University. Dr. Nuckols established and currently directs the Environmental Health Advanced Systems Laboratory in the Department of Environmental Health at Colorado State University. His primary research focus has been to develop exposure metrics for epidemiologic studies of pesticides in the environment and drinking water contaminants. Dr. Nuckols will be consulting 2 weeks of each month for a 16-month period. He is located in EPS 8121 and can be reached at 435-4711.

Ms. June Peters has joined the Clinical Genetics Branch as a genetic counselor. Ms. Peters holds master's degrees in both genetic counseling and psychological counseling and comes from the University of Pittsburgh, where she was an Assistant Professor of Human Genetics. Ms. Peters is located in EPS/7021 and can be reached at 594-7646.

In August, **Ms. Sandy Rothschild** joined the Office of Division Operations and Analysis, DCEG, as an epidemiology program assistant. Previously, Ms. Rothschild worked at the Center for Scientific Review, NIH, in the Technology Services Branch. She has completed course work at Montgomery College on web design and assisted in the development of the Center's internet and intranet sites. Ms. Rothschild is located in EPS/8066 and can be reached at 594-9895.

Dr. Maria Sgambati, a fellow in the Genetic Epidemiology Branch, has accepted a position as Scientific Editor for the cancerTrials website *http://cancertrials.nci.nih.gov/index.html* in the NCI Office of Education and Special Initiatives. We are sad to lose her but delighted that she has found a niche that suits her talents and experience well. She will be a great asset to her new colleagues.

Ms. Donna Strong is the new Personnel Management Specialist for the DCEG Administrative Resource Center. Previously, she was the Personnel Management Specialist for the Division of Clinical Sciences. She has over 20 years of government experience. Ms. Strong is located in EPS/8052 and can be reached at 594-7512.

In September, **Dr. Rebecca Troisi** joined the Office of the Director of the Epidemiology and Biostatistics Program as a staff scientist. She will be a project officer on the Diethylstilbestrol Study. Dr. Troisi previously served as a postdoctoral fellow in the Environmental Epidemiology Branch and later worked for Social and Scientific Systems, Inc., in Bethesda. Dr. Troisi is located in EPS/8105 and can be reached at 594-7833.

Mr. Roel Vermeulen has joined the Occupational Epidemiology Branch as a consultant from Utrecht University, The Netherlands. Mr. Vermeulen expects to have his Ph.D. in January of 2001, at which time he will become a postdoctoral fellow. His dissertation topic is on the dermal route of exposures to genotoxic agents among rubber manufacturing workers. At NCI, Mr. Vermeulen will be focusing on exposure assessment in occupational cancer epidemiology studies. He is located in EPS/8091 and can be reached at 402-9850.

Dr. Sophia Wang has joined the Interdisciplinary Studies Section of the Environmental Epidemiology Branch as a tenure-track investigator. Her research will focus on somatic and germline genetic aspects of DNA virus oncogenesis. Dr. Wang received a B.S. in biology from the Massachusetts Institute of Technology, where she conducted research on DNA adducts. After a few years as a molecular biologist in a biotech firm, she entered the Ph.D. program in chronic disease epidemiology at the Johns Hopkins University School of Hygiene and Public Health. Her dissertation focused on the interaction of aflatoxin exposure, hepatitis B viral infection, and the HPRT gene in the development of hepatocellular cancer. Since 1998, she has been an Epidemic Intelligence Service Officer at the Centers for Disease Control and Prevention. Dr. Wang is located in EPS/7072 and can be reached at 402-5374.

In August, **Ms. Elyse Wiszneauckas** joined the Office of Disease Control and Prevention, Office of Division Operations and Analysis (ODOA), DCEG, as an epidemiology program assistant. She will manage the Intramural Research Program Database, track the ODOA budget, and be involved in many special projects with the Office of the Director and ODOA staff. She is currently enrolled in undergraduate classes at Montgomery College and is pursuing a degree in Computer Information Technology with an emphasis on database administration. Before coming to DCEG, Ms. Wiszneauckas worked in the Division of Basic Sciences and in the Office of Management, NCI. Ms. Wiszneauckas is located in EPS/8059 and can be reached at 594-9891.

Dr. Xia Xu has joined the Environmental Epidemiology Branch as a postdoctoral Cancer Research Training Award fellow. Dr. Xu received his M.D. in 1987 from the Shanghai Second Medical University and his Ph.D. in toxicology in 1995 from Iowa State University. During postdoctoral training at the Department of Food Sciences and Nutrition at the University of Minnesota, he developed novel methods for assessing complete endogenous estrogen metabolite profiles and estrogen-DNA adducts and for relating them to human breast cancers. In addition, he has investigated the effects of isoflavones and lignans on reproductive hormones. Currently, he is developing laboratory capabilities to enhance efforts of the Division to understand the etiologic role of endogenous hormones and DNA adducts. He is located in EPS/7082 and can be reached at 402-7482.

Dr. Rose Yang has joined the Genetic Epidemiology Branch as a visiting fellow. Dr. Yang came to the United States from Beijing in 1994 and received her Ph.D. in physiology and biophysics from Georgetown University Medical Center in 1999. Her thesis project involved analyzing the role of the antimetastasis tumor suppressor gene *KAI-1* both *in vitro* and *in vivo*. Before joining the Branch, Dr. Yang spent 9 months at the Lombardi Cancer Center. At NCI she is working on gene mapping of chordoma in conjunction with Dr. Dilys Parry and Dr. Alisa Goldstein. She is also working on linkage analysis of data from melanoma families and from families with the nevoid basal cell carcinoma syndrome. Dr. Yang is located in EPS/7005 and can be reached at 594-7804. ■