DCEG Linkage

Division of Cancer Epidemiology and Genetics

National Cancer Institute

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ENTERING THE 21ST CENTURY SIDE BY SIDE: EPIDEMIOLOGY AND GENETICS

Editor's note: *In this edition of* Linkage, *Dr. Fraumeni has relinquished the Director's Page in order to feature the research visions of the Division's Program Directors, Dr. Hoover, Director of the Epidemiology and Biostatistics Program (EBP), and Dr. Knudson, Acting Director of the Human Genetics Program (HGP).*

The steadfast focus of Dr. Hoover and Dr. Knudson on melding genetics and epidemiology has put DCEG at the forefront of these disciplines. Following are their research visions that position DCEG for the next millennium.

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Epidemiology and Biostatistics Program

Robert N. Hoover, M.D., Sc.D.

"The Program's vision mirrors that of the Division," says Dr. Hoover. "Part of this derives from the fact that, until recently, the current Division was the Program. However, part of the similarity derives from the very nature of epidemiology. It calls for a large, broad-based program that affords investigators the opportunity and resources to go where there is a 'natural experiment.' These rare events require studies of very large groups of people on location. This sort of opportunity tends to mandate the need for a national program."

As Director of a Federal program, Dr. Hoover believes that we have to be alert to emerging public health problems and respond to them quickly. He says the Federal Government is frequently called upon and expected to have the answers to a variety of health-related questions. Thus, the Program cannot afford to specialize in one area but must be actively involved in all of the major areas of cancer epidemiology. Due to its size and national perspective, the Program is expected to take the lead in particularly difficult epidemiologic issues. Dr. Hoover and his staff can generally tackle these issues by undertaking studies entirely by themselves, or by putting together large national or international studies involving people with the complementary capabilities to address the problem and providing a platform for them to work with one another.

"We pride ourselves on doing this," says Dr. Hoover, "and we're good at it, having done it for many years." It also helps that the Division is in the position to know about and have access to national resources like the Social Security Administration, the National Center for Health Statistics, the Department of Agriculture, and other places where data are collected. NCI investigators are also free to pursue high-risk

and long-term studies without jeopardizing their careers.

Because NCI orchestrates efforts to address difficult issues and has a national perspective, it also has a responsibility to pay particular attention to problems or questions that might otherwise go unattended, says Dr. Hoover. For example, not many people would care to investigate the high rates of lung cancer in Glynn County, Georgia, or colon cancer in David City, Nebraska, which were identified by the cancer mortality atlas. Since there is no concentration of chronic disease epidemiologists in these areas, NCI needs to target studies at sites where these unusual disease occurrences might otherwise go unattended and unnoticed. In addition, because of its national position, the Program is able to collaborate with other governments to study unusual cancer risks or exposures in various countries.

NIH is predominantly a laboratory research facility and, having grown up in that environment, DCEG is in an ideal position to lead in the area of interdisciplinary studies. Being immersed in the largest basic science program in the world, according to Dr. Hoover, gives the Division the opportunity to interact and collaborate with various kinds of laboratory scientists.

"These views of epidemiology in the government setting have led to our creation of a broadly based group with rapid response capabilities, an ability to exploit opportunities otherwise unaddressed, a responsibility to tackle particularly difficult and high-risk studies, and a capacity to focus on collaborative interdisciplinary studies," says Dr. Hoover.

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The development of the Human Genetics Program as a companion initiative, and Dr. Klausner's enthusiasm for NCI to become the world's leader in molecular epidemiology, are recent events contributing to strengthening the Division and Institute programs in genetics and molecular epidemiology, and in projects aimed at clarifying gene-environment interactions.

Important Developments

The Program has been responsible for numerous advances over the last 30 years. One of the earliest and most notable was the discovery in the late 1960's by Dr. Fred Li and Dr. Joseph Fraumeni of a series of families prone to diverse forms of cancer, most often childhood sarcomas and breast cancer, known today as Li-Fraumeni syndrome. The families in these studies have been evaluated periodically, and because of new technologies made available in the late 1980's, the cause of this rare syndrome was identified as a germline mutation in the *p53* gene. While the syndrome may not have broad public health significance, *p53* clearly has major implications for common cancers in the general population and in our understanding of the basic mechanisms of human carcinogenesis. As a major tumor suppressor gene, *p53* serves as a central "watchdog" gene that polices aberrant cells.

Dr. Hoover says that the Program was also responsible for being either the first or among the first to observe the following: (1) that estrogen medication is a causative factor in breast cancer; (2) that there is an association between herbicide use and non-Hodgkin's lymphoma; and (3) that fruit and vegetable intake protects against tobacco-related cancers. The Program was also the first or among the first to identify (1) HTLV as an oncogenic virus in human populations, and (2) the particular susceptibility of the young to radiation-induced breast and thyroid cancers.

Program staff have also made significant advances in the development of methods and techniques that have improved the way cancer epidemiology is conducted. The first occupational linkage system was developed in the late 1970's by Dr. Shelia Zahm and became the prototype for assessing exposures in occupational epidemiology. Historically, NCI has been the place for the development of statistical methodologies to conduct multiple contingency table

analyses, and for modifications to regression techniques that make these particularly strong tools for epidemiologic investigations. In addition, new types of studies have been developed or refined by Program scientists, like the case-cohort study and the kin-cohort study.

Evaluation of Program

"One of our biggest success stories is how the Program has changed the way epidemiology is conducted by modernizing and bringing it into the 21st century," says Dr. Hoover. He recalls that, years ago, investigators developed questionnaires, coded records, hired interviewers, supervised field workers, etc. These activities did not leave much time for epidemiology. The Program introduced a new concept of hiring people who are trained in these specific activities, thus freeing the epidemiologist to do epidemiology. Dr. Hoover says, "The concept of support services through contracts revolutionized how epidemiology is conducted, allowing more to be done, more quickly, and the entire field has followed our lead."

Another feather in the Program's cap has been the happy marriage of laboratory science and epidemiologic studies. "They complement each other, and the opportunity to do them together, to circumvent the problems of both, has been a major success story," says Dr. Hoover.

The Future

Dr. Hoover believes the greatest challenge is to maintain the pace of innovation in epidemiology and not to become complacent. For example, the promise of molecular epidemiology is reflected in the fact that epidemiology is the noun and molecular is the adjective. "I believe that studies in this field need to be led by epidemiologists, and not by the many researchers who lay claim to molecular epidemiology. Ultimately, the promise of the field will only be realized by work which is high-quality epidemiology."

Dr. Hoover feels there needs to be a balance in research programs with respect to both subject matter and methodology. "In our current rush to take advantage of opportunities in molecular epidemiology, we need to remember there are proven traditional epidemiologic methods that have produced and will continue to produce major findings in public health. With respect to subject areas of research, our historically strong program of family studies has put DCEG in good stead to lead the rapidly expanding field of genetic epidemiology. However, just as we maintained a strong genetics program when enthusiasm was high for the rapid development of our environmental epidemiology programs, we need to continue to maintain a balanced and comprehensive approach that pursues all areas of opportunity. We need to continue our leadership in investigating the occupational, nutritional, lifestyle, radiation, infectious, and other environmental causes of cancer, while intensifying collaborations to utilize new technology in genetics to help identify environmental carcinogens and gene-environment interactions." ■

Patricia S. Evans

The Human Genetics Program

Alfred G. Knudson, Jr., M.D., Ph.D.

"The largest advances in science often come when you least expect them," says Dr. Alfred Knudson, Acting Director of DCEG's Human Genetics Program. "When you specify everything you're going to do in a plan, it tends to diminish opportunities for major breakthroughs. Some research should be open-ended, indicating that we haven't reached the point where we can prevent or treat all cancers successfully every time. Sometimes researchers declare war on cancer as if they are building an atom bomb or going to the moon. They forget that we do not yet have the basic knowledge required by those projects."

Discussing HGP apart from the Division itself is difficult, says Dr. Knudson, because genetics is a pervasive feature of cancer, just like the environment. Investigators working on environmental studies have become very involved in genetic factors that might influence the response from an environmental agent. In the same way, HGP is very interested in environmental modifiers of genetic determinants. Dr. Knudson says that most cancer investigators understand that there is some element of chance here,

because mutations can occur without any known cause and in a random fashion, but the probability of mutations can be increased by the inheritance of predisposing genes and by certain exposures. Although there are cancers that will always occur because of spontaneous mutations, about 80 percent of cancers are thought to be associated with environmental exposures, preexisting genetic conditions, or both. HGP is concentrating on trying to identify predisposing genes and understand how their interactions with environmental exposures affect risk.

Important Developments

The work of Dr. Peggy Tucker and Dr. Jeff Struewing (HGP) in collaboration with Drs. Patricia Hartge and Sholom Wacholder (EBP) on *BRCA1* and *2* has been very important. One of the major findings is that there is variation in susceptibility from these genes resulting from environmental factors or other genes. "If someone in a cancer family asked us what his or her chances are of getting cancer, we have imprecise answers," Dr. Knudson said. "Based on the *BRCA* work, we now suspect that there is quite a range of risks, and that we need better answers than we have now."

The interaction of heredity and environment is well illustrated by skin cancer. The discovery of the patched gene for the rare nevoid basal cell carcinoma syndrome was a major finding with important implications for understanding the very common nonhereditary basal cell carcinomas. The collaboration of Dr. Alisa Goldstein of HGP with Dr. Michael Dean from the Laboratory of Genomic Diversity in the Division of Basic Sciences made this discovery possible. "Nevoid basal cell carcinoma is a rare syndrome, but if you look at the garden variety basal cell carcinoma in people who don't have this syndrome, they also show patched gene mutations, which are acquired after birth," says Dr. Knudson. For both groups, the risk of skin cancer is increased by sunlight.

Are there people who vary in their susceptibility to environmental factors? The probability of a black person getting sun-related skin cancer compared to a white person is small, while the probability of a white person who moves from England to sunny Australia getting skin cancer is high. "We know some answers," says Dr. Knudson, "so it is not a surprise that the environment does not fall evenly on all people." However, sometimes susceptibility is much more subtle. For example, people have different ways of metabolizing environmental chemicals, a research area of great interest to Dr. Neil Caporaso. Since some people appear to be particularly susceptible to tobacco-induced lung cancer, while others are resistant, it may be possible to develop interventions by identifying the mechanisms affecting risk.

Evaluation of Program

"Our Division is interested in populations of people with cancer," says Dr. Knudson. "Sometimes we can study them by focusing on high-risk families; at other times, it's better to look at their environmental exposures. The *BRCA1* and *2* study is an example of Division-wide collaboration, with an evaluation of both genetic and environmental risk factors. The HGP and the EBP work together, not only because we are interested in what the other is doing, but because one group alone cannot solve many of the cancer riddles. In this vein, the HGP is expanding to acquire more expertise in the area of translational research through which our genetic findings can be applied to clinical practice and counseling. In addition, the HGP has created a Laboratory of Population Genetics, which is being headed by Dr. Kenneth Buetow, that will be critical to our ability to identify susceptibility genes and gene-environment interactions."

The Future

What are the problems facing cancer genetics? How can genetics help us to understand cancer, with respect to both the influence of the genes themselves and the influence of the genes in response to the environment? The genetics of cancer, in which the Division of Basic Sciences has great expertise, concerns cells. The genetics of cancer also concerns the individual (i.e., the person who develops cancer), which is the interest of the Division of Clinical Sciences. In addition, the genetics of cancer concerns populations, which is DCEG's main focus. To study the genetics of cancer, one must consider many areas, which means collaborating with other groups. "We have always shared ideas across NCI. None of us works in a vacuum, nor can we afford to do this," says Dr. Knudson. "Divisions were not created to 'divide and conquer,' but for convenience, so things don't get massive and out of control."

To ensure that there are properly trained scientists in the field of cancer genetics, HGP has begun an interdisciplinary training program for postdoctoral fellows. Coordinated by Dr. Dilys Parry, the program is designed for persons who are acquainted with epidemiology, statistics, laboratory research, or clinical oncology, but who wish to have a broad working knowledge of all approaches and their relationship to genetics.

"A lot has been accomplished in the prevention and treatment of cancer, but still there is a significant upward trend in the incidence of certain cancers," says Dr. Knudson. "We know, for instance, that melanoma is on the rise, because people are increasingly exposed to the sun's rays, while other tumors are increasing for reasons that are unclear. Lung cancer keeps rising in women, although rates are leveling off in men, because a high percent of people still smoke. On the other hand, there is a reduction in some cancers, such as the stomach, which continues to go down in incidence and in mortality.

"For some reason," says Dr. Knudson, "our best record for cancer treatment seems to be for the rare ones. Seventy-five percent of cancers in children are cured. Young men with testicular cancer are cured at an astonishingly high rate. Successes were unheard of when I was a medical student. We've come a long way, but the common cancers still hang on."

Dr. Knudson feels that new ideas are needed for treatment, early diagnosis, and prevention of many cancers, especially pancreatic, colon, ovarian, breast, and prostate cancer. The prospects are better for cancer patients, but people are still dying in great numbers from these terrible diseases. If scientists could figure out the major differences between a cancer cell and a normal cell, according to Dr. Knudson, it might then be possible to correct the cancer cell or kill it selectively. "If we could deactivate or control the progression of malignant cells, we could extend many lives before the critical genetic mutations take over," says Dr. Knudson. "The goal now may not be to eliminate all cancers, but rather to enable people predisposed to cancer to get it 20 years later than is usual now. This could result in dramatic improvements over the current situation. I think both Dr. Hoover and I operate on the idea that cancer is something that will always be with us, because cells make mistakes when DNA is replicated. It's a cruel hoax to say we will eliminate all cancer. Just shifting age curves for cancer significantly would make a big difference. There are people who die of lung cancer without ever having smoked, but they die 20 to 25 years later than smokers do. Prevention is the watchword here. For other cancers, early diagnosis may be a rewarding approach. For example, if colonoscopy could accomplish this for colon cancer, we need to make it less expensive and available to all. Our basic aim should be to operate at every level, and keep our base of knowledge growing so that we can discover more ways to keep people alive, and in good health." ■

Patricia S. Evans

TITLE 42 IN A NUTSHELL

Title 42 is not the name of a new golf ball, restaurant, or latest best seller, but is part of the U.S. Code of Federal Regulations dealing with Public Health and Welfare. Around here, the most bandied about sections are 209(g) and 209(h), and for those cognoscenti who want to delve deeper, try *http://www.fas.org/irp/offdocs/laws/usc42.html*. Actually, we have been using Title 42 for years, since it is the authority under which we bring people on board into time-limited FTE-bearing appointments, such as tenure-track investigators, staff fellows, and visiting scientists and associates.

What is new is the expanded use of Title 42 for recruiting highly talented and experienced scientists into the intramural and extramural research programs. Although these appointments are still time-limited, the initial period and subsequent unlimited renewals may be for as long as 5 years. This new use of Title 42 will make us more competitive with respect to salary, and reduce the time and rigamarole for bringing someone on board. The annual stipend begins at the GS–13 level, and goes as high as Executive Level I (currently $151,800). Of course, the higher the stipend, the higher the level required for approval (Executive Level I needs the NIH Director's blessing). However, stipends ranging up to Executive Level IV (currently $118,400) can be approved by Institute Directors, who may redelegate the authority to Scientific Directors.

This new use of Title 42 complements the Senior Biomedical Research Service (SBRS) and the Senior Executive Service (SES). Although each of these personnel mechanisms permits salaries above those allowed under the General Schedule of the Civil Service, both the SBRS and SES have a limited number of positions. Expanded use of Title 42 not only avoids that restriction but it offers greater flexibility at the programmatic level than these other mechanisms for recruiting and retaining key individuals.

Besides allowing the recruitment of highly sought-after talent, Title 42 can also be used to hire staff scientists to carry out projects with specific goals, such as setting up and operating a facility, and to retain PHS Commissioned Officers upon their retirement from the Corps. In addition, Civil Service workers who have maxed out at GS–15/10 may be converted to Title 42 to obtain higher salaries. Like other appointments under Title 42, employees receive government benefits (e.g., creditable service toward retirement, contributions for health insurance and pension, and participation in the Thrift Savings Plan), but do not have the job protection or permanency afforded under Civil Service.

Although all the policy and administrative wrinkles still need to be ironed out, we are hopeful that this expanded use of Title 42 will become an effective recruiting mechanism for enhancing the Division's scientific staff. Stay tuned. ■

Jim Sontag

CANCER MAPPING: CHARTING A COURSE FOR HUMANKIND

People have always been intrigued by maps. These flat graphic representations of the earth or sky represent travel, exploration, and history. They are the source of planning and dreaming. They get us from point A to point B. The earliest maps that have survived are from Babylon and Egypt from around 2500 B.C. Just as these maps give us a look at history, cancer mortality maps allow us to visualize the patterns of cancer in various parts of the country.

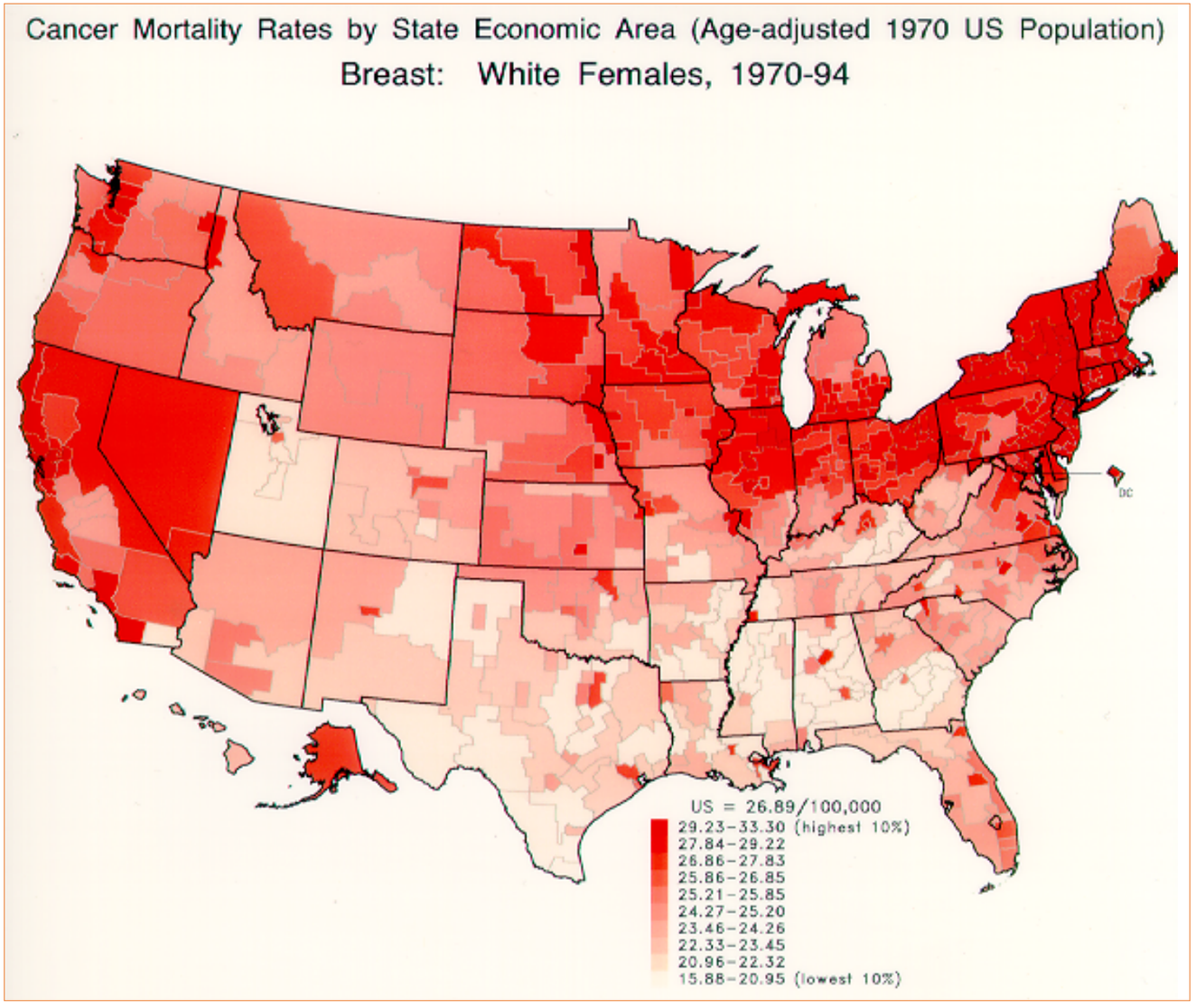
NCI's first cancer mortality maps were published in two separate atlases. The first was published in 1975 as the *Atlas of Cancer Mortality for U.S. Counties: 1950–1969,* which was for whites only; and an *Atlas of Cancer Mortality Among U.S. Nonwhites: 1950–1969* was published in 1976. Subsequent atlases were published in 1987 and 1990. Maps from these atlases identified a number of "hot spots" around the country for various cancers, which led to correlation studies with demographic and environmental variables to help formulate etiologic hypotheses. This led, in turn, to case-control studies in high-risk areas.

"These early atlases stimulated much analytic research," says Dr. Susan Devesa, Chief of the Descriptive Studies Section in the Biostatistics Branch, whose responsibility it is to update the atlases. In 1994, NCI began looking at ways to revise the atlases that would best serve researchers, the target audience. "We gave a lot of thought to how best to develop these maps, such as statistical methodology, colors, and presentations," said Dr. Devesa. "We wanted to make sure that these atlases would be giving researchers the information they need to execute their work."

Dr. Devesa asked a member of her staff, Mr. Dan Grauman, a computer specialist, to develop the approaches to create the maps. Mr. Grauman's background in mathematics and statistics made him a natural to take on this task. In addition, Mr. Grauman looked for sources of funding for the creation of an Internet web site for the atlas. His efforts yielded $80,000 in funding from the National Performance Review Innovation Fund (NPRIF) at the Department of Commerce.

"We get death counts for each county each year for every type of cancer across the country from the National Center for Health Statistics. We had the complete statistics for years 1970 to 1992," says Mr. Grauman. The exceptions are Alaska and Hawaii, for which data are provided only at the state level.

As Mr. Grauman developed the maps, Dr. Devesa began writing the text in collaboration with Drs. Fraumeni and Hoover, as well as with Dr. William Blot, the former Chief of the Biostatistics Branch. Toward the later stages of the project, additional data were made available, and NCI made the decision to expand the maps through 1994 to encompass 25 years. Corresponding maps for 1950 to 1969 will also be included, as appropriate.



What's New This Time?

"This is the first time we will present data for the black as well as white populations," says Dr. Devesa. The earlier atlases presented data on nonwhites as a group. Most of the maps will present rates for the State Economic Areas (SEA), which are individual or groups of counties defined by the Census Bureau. For the more common cancers, maps at the county level will also be presented for whites.

The more than 140 maps, plus tables and text, will be available on DCEG's Internet web site. "These will be *static maps*," says Mr. Grauman, "which means the user cannot change any of the map parameters. It's a 'what you see is what you get' format." Dr. Devesa and Mr. Grauman believe the site will be used mainly by researchers, who will be able to download files as needed. The database cannot be searched, but all county or SEA rates can be identified for a particular cancer site or geographic location.

An interactive site for a more general audience is already being planned with *dynamic maps*. This site will contain the entire United States by county and/or SEA, as does the static map web site, but it will also include statewide data. The user will be able to control parameters, such as zoom, pan, and color, and make quantile selections. "Also," says Mr. Grauman, "users will be able to type in their zip code and get the cancer rates for their county and

comparison rates for their state and the United States." Nothing will be downloadable from this site, but searches can be done.

Dr. Devesa says the new atlas should be ready by the fall, and that she is working with the NCI Office of Cancer Communications on the distribution of the atlas and notification of those groups that would be interested in this type of information—like other government agencies, state health departments, and cancer centers.

"It is our hope," says Dr. Devesa, "that these maps will stimulate interest on the part of researchers to find creative ways to help us learn more about the geographic patterns of cancer mortality and risk factors contributing to these conditions." ■

Patricia S. Evans

THANK YOU, DR. KLAUSNER

On behalf of the staff of the Division of Cancer Epidemiology and Genetics, the DCEG Committee of Scientists would like to express our gratitude to Dr. Richard Klausner for his participation in our recent Town Meeting. The meeting was inspiring, encouraging, and enjoyable. We appreciated the knowledge, enthusiasm, and optimism about the opportunities in cancer research that he communicated to us. We are also grateful for his willingness to address, in a thoughtful manner, the diverse concerns raised by DCEG staff. It helps us to have perspective about some of the issues we all face. We hope that Dr. Klausner will consider returning and making the Town Meeting an annual event. Thank you. ■

Sholom Wacholder
Chair, DCEG Committee of Scientists

RESEARCH VISION

Nutritional Epidemiology Branch

As members of the newest Branch in the Epidemiology Program, we are in the process of establishing research priorities and sharing our diverse backgrounds and interests, which span nutrition, epidemiology, biochemistry, and molecular biology. Although diet and nutrition are believed to be related to a majority of human cancers, most of the specific causal and protective factors remain to be identified. Their elucidation is complicated by their interrelationships with each other and with other lifestyles. However, the influence of diet and nutrition on cancer etiology is pervasive, and most of the exposures are modifiable. We are excited by the challenges before us.

Like the other intramural epidemiology branches, we have the responsibility to provide scientific leadership, conduct higher risk and more difficult studies, develop and take advantage of national and international resources, and provide needed methodologic research. Our interests and expertise are broader than just diet and nutrition, encompassing, for example, anthropometry, physical activity, and endogenous hormones and growth factors. Because of the extensive biological research underlying contemporary nutrition, we are especially interested in multidisciplinary studies with metabolic and/or molecular components.

There is the possibility of biases in dietary and nutrient information collected after cancer diagnosis has been widely discussed, and we plan to balance the large number of retrospective analyses in which we are now involved with more prospective studies. We can take advantage of the several cohorts in the Division on which we are working, such as the PLCO, AARP, Radiation Technologists, Agricultural Workers, and BCDDP cohorts. We feel that variability in exposure facilitates and strengthens dietary studies, and hope to engage in more studies utilizing migrant populations and international differences, such as the Asian-American study of breast cancer, the Polish study of stomach cancer, and a study of cooking practices in the European Prospective Investigation on Cancer and Nutrition.

Much of the methodology that has been developed for nutritional epidemiology has relied more heavily on statistics than biology. Although these efforts have been productive, we are excited about continuing our collaborations with the biostatisticians in the Division to develop biologically meaningful approaches. Chemoprevention trials have dominated NCI research in the area of diet and cancer over the past 15 years; a more reasonable balance is necessary. We recognize the complexities of this approach, and hope that our epidemiologic work will increasingly contribute to the scientific bases for decisions about future trials. In addition, we are continuing followup of the Colorectal Polyp Prevention Trial, in which participants were randomized to different diets rather than supplements.

More specifically, we will continue our focus on vegetables, fruits, and micronutrients—trying both to answer public health questions about the protective effects of vegetable and fruit intake as well as to identify the active nutrients and/or phytochemicals. We are evaluating the roles not only of the "antioxidant micronutrients," but also of folate and other B vitamins involved in methyl metabolism, which are essential to nucleic acid synthesis and repair. We are intrigued by the challenging area of energy balance, which involves caloric intake, physical activity, metabolic efficiency, and body size and shape, and are aware that this is a rarely evaluated, but probably a very important, exposure in the etiology of breast and other cancers. In our research, we will be increasingly treating body size and shape as variables that change during adult life.

Because of their extensive use in the United States, physiologic and pharmacologic dosages of nutrient supplements, botanical, and specific food additives, such as artificial fats and sweeteners, will continue to be evaluated. Two additional research areas into which the Branch is expanding are the effects and mechanisms of alcohol intake and the importance of early life exposures. Nutrition-genetic interactions are a promising area because of the high prevalence of exposure to dietary factors, the expanding opportunities to assess genetic factors, and the limited research already completed. We have been actively studying several carcinogens produced during meat preparation and genetic determinants of their metabolism. Folate, alcohol, and obesity are other specific areas where we are integrating diet and genetics. We also want to look systematically at the various cancers to determine (1) which may have been neglected in terms of dietary studies, such as the lymphatic and hematopoietic cancers or early childhood cancers; and (2) how universal certain dietary effects are, such as the protection offered by vegetable and fruit intake. Efforts continue to evaluate and improve dietary assessment methods, specific nutrient assays, and hormone and growth factor measurement.

Because of our strong interest in diet, we feel it is critical to initiate epidemiologic studies in which nutrition is the major focus, and not always to rely on generic dietary assessment instruments being added to epidemiologic studies with multiple objectives. We want to continue our multiple collaborations with our colleagues in other branches, and wish to be actively involved in the design, analysis, and interpretation of studies, as well as in the development of dietary assessment instruments and administration of laboratory components. We feel that our understanding of the biological basis of nutrition, metabolism, and physiology provides an important contribution to epidemiologic work. We recognize that we are a small Branch and cannot always provide the expertise needed for the many projects with nutrition components currently underway. Yet we hope, in the future, to be responsive and to be involved in any major nutrition efforts initiated within the Division. ■

Regina Ziegler

Occupational Epidemiology Branch

The Occupational Epidemiology Branch conducts epidemiologic investigations in the workplace and other settings in which high exposures to occupational and environmental agents occur. Our overall philosophy is to meld epidemiology, quantitative exposure assessment, and biologic and genetic components in investigations to identify chemical causes of cancer, to develop a better understanding of carcinogenic mechanisms, and to improve epidemiologic resources for use in epidemiologic research.

Several investigations with this interdisciplinary orientation are underway. (1) A large case-control study of bladder cancer (1,500 cases and 1,500 controls) in Spain combines, for the first time in a

study of this cancer, the use of a sophisticated questionnaire for assessment of occupational exposure. This questionnaire was recently developed by Branch industrial hygienists along with a molecular component to investigate gene-environment interactions. (2) An extension of the investigation of 75,000 benzene-exposed workers in China is designed to evaluate risks of leukemia and non-Hodgkin's lymphoma over a wider range of benzene exposures than previously possible; and to determine whether preneoplastic outcomes observed among workers with benzene poisoning also occur at lower exposure levels. (3) A prospective cohort study of 90,000 women in China provides an unusual opportunity to investigate occupational and environmental exposures because of the large number of women who work in industry and the heavy environmental pollution in the study area. Collection of blood and urine from a large fraction of the participants will be used to determine body burdens for important occupational and environmental exposures and to assess gene-environment interactions. (4) A retrospective cohort study of 8,000 miners is designed to evaluate the risk of lung cancer from exposure to diesel exhausts. This investigation will provide crucial information on an exposure that is common among the general population. Miners have exposures, in order of magnitude, higher than any other occupational group and present an unusual research opportunity to clarify the carcinogenicity of this exposure. The study employs a biospecimen component to relate metabolites of diesel exhausts in blood and urine with indicators of biologic effects and a computerized exposure assessment program recently designed by the Branch investigators for use in the development of quantitative exposure assessment. (5) The Agricultural Health Study is an ongoing investigation of over 90,000 pesticide applicators and their spouses designed to investigate the role of pesticides and other agricultural exposures in the development of cancer and other chronic diseases. During the next 5 years, the cohort will be linked with vital statistics and tumor registries to obtain information on cause of death and diagnoses of cancer. All participants will be contacted for an interview to obtain additional information on agricultural exposures and other cancer risk factors, and to collect buccal cells for assessment of gene-environment interactions.

We intend to expand our efforts in the study of general environmental exposures and the study of interactions with occupational exposures and other risk factors. In particular, we seek opportunities in which occupational and environmental exposures to suspected carcinogens can be evaluated in the same study. Such investigations would allow us to evaluate cancer risks over a wider range of exposures than is possible in studies focusing on only occupational and environmental routes. They would also provide direct information on a larger segment of the population. Occupational and environmental exposures to the same agent often form a continuum, with the lower levels of occupational exposure overlapping with the upper end of general environmental exposures. This overlap can help to overcome difficulties associated with epidemiologic studies in the environmental arena. Exposures of current interest that might be amenable to this dual approach include: nitrates and cancer (occupational exposures to farmers and general population exposures in drinking water), and pesticides and cancer (evaluation of occupational exposure in applicators and exposures of the general population by remote sensing and GIS).

Because of a reliance on the cohort design, occupational investigations in the past have often neglected other risk factors, such as diet, tobacco, alcohol, microbes, and genetic factors. Even when nonoccupational factors were included in an investigation of workplace exposures, the purpose was usually to evaluate confounding. The ability to control for confounding is important. An even stronger argument to obtain information on nonoccupational factors in investigations of workplace exposures may be the opportunity to evaluate the potential for effect modification. We have recently had several clues to interactions that deserve further evaluation, such as studies of non-Hodgkin's lymphoma in relation to serum PCB levels, Epstein-Barr virus infection, nitrates in the drinking water, and dietary factors. ■

Aaron Blair

Radiation Epidemiology Branch

The Radiation Epidemiology Branch (REB) conducts research to identify and quantify the risk of cancer in various populations exposed to ionizing and nonionizing radiation. Emphasis is placed on evaluating the risk of radiation-associated cancer in terms of tissues at risk, dose response, characteristics of the radiation exposure, and possible modifying influences of other environmental and host factors. Because many REB studies involve irradiated cancer patients, the Branch investigates the etiology of second cancers, including the role of chemotherapy agents alone or in combination with radiotherapy. Recently, we have become more involved in research on the molecular characterization or "fingerprints" of radiation-related tumors, and on the variation in radiogenic risk associated with cancer susceptibility genes.

In the area of ionizing radiation, we are investigating the cancer risk following radiation exposures from medical sources such as diagnostic and therapeutic irradiation, including radiotherapy in combination with chemotherapy and related drugs. We are evaluating occupational exposures, focusing on high- and low-dose protracted exposure to external and internal radiation, as well as environmental sources, particularly from the atomic bombings in Hiroshima and Nagasaki, residential radon, nuclear waste, and nuclear testing. Over the last few years, REB has been shifting its emphasis toward occupational and environmental exposures, while expanding its research program on multiple primary cancers. In addition, the public and scientific interest in the long-term health effects from exposures to nonionizing radiation has increased substantially over the last decade. Results from epidemiologic studies have been inconsistent, and interaction mechanisms, particularly at the cellular level, are not understood. REB is conducting comprehensive epidemiologic investigations of childhood leukemia and adult brain cancer which should improve our understanding of the relationship between nonionizing radiation and carcinogenesis.

Over the next few years, REB will be focusing on several high-priority research areas in carcinogenesis: evaluation of the effects of radioiodines, chronic and low-dose radiation exposures, new chemotherapy, and radiotherapy regimens in treating cancer; the interplay between radiation and other exposures; the role of host susceptibility in radiogenic tumors; the effects of exposure to nonionizing radiation; the integration of new physical and biological methods for measuring radiation exposures; and methods for incorporating uncertainties in dose estimates in dose-response analyses. We also have identified three specific programs for future emphasis: UV and skin cancer, childhood cancers, and gene-radiation interactions. These projects will be conducted in collaboration with the Genetic Epidemiology and Biostatistics Branches.

Skin cancer is the most common cancer in white populations worldwide, and the incidence of both melanoma and nonmelanoma skin cancer has increased over time. Sun exposure is a well-documented cause of melanoma and nonmelanoma, but neither the patterns of risk nor the quantitative relationships are well described. We are planning several epidemiologic studies on nonmelanoma skin cancers, including an evaluation of time trends, and incidence patterns in terms of age, ethnicity, gender, sun exposure, body location, and histopathology. Case-control studies will be conducted to evaluate risk factors, including sun exposure patterns, skin type, use of sun screens, chemical exposures, diet, occupation, medical history, residential history, family cancer history, ethnicity, and genetic susceptibility. In particular, we are planning molecular epidemiologic studies on the mechanisms of genetic susceptibility on the carcinogenic effects of ultraviolet radiation (e.g., *PTCH* and DNA repair genes).

Despite four decades of extensive investigation, the etiology of childhood cancers is poorly understood. We have the opportunity to increase our understanding of these important cancers by extending and expanding our ongoing descriptive research, as well as conducting new analytic studies initializing national registries in Sweden and clinical trial groups in the United States. In addition, ongoing studies of childhood cancer survivors will provide some insights into the risks and determinants of late effects, including second cancers.

Several of the obstacles that make conducting studies of gene-environment interactions so difficult can be minimized by studying individuals exposed to ionizing radiation. The relatively accurate radiation exposure estimates reduce misclassification, while the

heterogeneity of exposure increases the statistical power to detect interactions. Because large numbers of people are needed to assess interactions, the large cohorts of irradiated individuals already under study are prime candidates for these types of investigations. Furthermore, groups with high attributable risks often can be identified. REB has been striving to take advantage of the special characteristics of radiation exposure for study of gene-environment interactions, but we need to seize additional opportunities. Currently, we are conducting population-based studies of ataxia-telangiectasia (AT); exploring the interaction between radiotherapy and the *Rb1* gene in a cohort of sporadic and familial retinoblastoma patients; searching for specific mutations in the *p53* gene among patients developing second cancers; looking for *NF2* mutations in irradiated patients who develop schwannomas of the head and neck following irradiation; and analyzing *BRCA 1* and *2* mutations in x-ray technologists who were diagnosed with cancer at an early age or who developed two or more primary cancers. We also want to expand our investigations of cancer risk in AT patients and heterozygotes, and in x-ray technologists. In addition, we are considering evaluating other REB-accessible study populations in our search for opportunities to investigate genetic interactions in radiogenic tumors.

To improve communications and to plan for the future, we have founded a journal club, established a second cancer working group and close collaborations with genetic epidemiologists and molecular geneticists, and initiated meetings with radiation researchers in other fields to discuss possible new directions for REB. We are also making efforts to expand our collaborations with other branches, divisions, institutes, agencies (e.g., Centers for Disease Control [CDC]) and extramural centers. Finally, we are striving to develop a radiation epidemiology training program at NCI that would allow fellows to spend 2 years at the Radiation Effects Research Foundation in Hiroshima, Japan. ■

Elaine Ron

SCIENTIFIC HIGHLIGHTS

Genetic Epidemiology Branch

Germline *CDKN2A (p16)* mutations have been detected in approximately 25 percent of melanoma-prone families. However, other genetic and/or environmental factors likely influence disease expression. To identify these factors, we evaluated the risk of melanoma in relation to clinical, environmental, and genetic factors in 13 American families who had germline *CDKN2A* mutations that cosegregated with melanoma.

Logistic regression analysis conditioning on family membership revealed that complexion, dysplastic nevi, total number of nevi, and solar injury each showed a significant association with melanoma, even after adjustment for *CDKN2A* mutation. Although *CDKN2A* mutations confer substantial risk for melanoma, sun-related exposures appear to further enhance the risk. Identification of these clinical and environmental factors should assist in further reducing the risk of melanoma in susceptible families with *CDKN2A* gene mutations. (Goldstein, AM; Falk, RT; Fraser, MC; Dracopoli, NC; Sikorski, RS; Clark, WH, Jr; Tucker, MA. "Sun-related risk factors in melanoma-prone families with *CDKN2A* mutations," *J Natl Cancer Inst* 1998; 90:709–11.) ■

Lea Harty

Environmental Epidemiology Branch

Dr. Montserrat Garcia-Closas is working on a study entitled "Interactive effects of genetic susceptibility and environmental factors on breast cancer risk: A population-based study." In April, she began the collection of buccal cell specimens from approximately 5,500 cases and 5,500 controls participating in an ongoing case-control study of breast cancer in the states of Wisconsin, Massachusetts, and New Hampshire. This study will evaluate genetic determinants of breast cancer and their interactions with environmental and reproductive risk factors, focusing on polymorphisms in enzymes involved in estrogen synthesis and metabolism.

Dr. Joanne Dorgan and her colleagues recently published a paper suggesting a protective effect of

carotenoids, specifically lutein-zeaxanthin and lycopene, for breast cancer. (Dorgan, J; Sowell, A; Swanson, CA; Potischman, N; Miller, R; Schussler, N; Stephenson, HE. "Relationships of serum carotenoids, retinol, alpha-tocopherol, and selenium with breast cancer risk: Results from a prospective study in Columbia, Missouri [United States]," *Cancer Causes Control* 1998; 9:1, 89–97.)

Data collection for NCI's follow-up study of women with augmentation mammaplasty has recently been completed. This retrospective cohort study identified nearly 13,500 women with cosmetic breast implants and 4,000 comparison subjects from 18 plastic surgery practices in 6 geographic locations. Drs. Louise Brinton, Lori Brown, and Jay Lubin are currently involved with data analyses. A special advisory group, headed by Dr. Mimi Yu, recently met to review the study design and advise on approaches to analysis, interpretation, and dissemination of the data. An ancillary study has recently been initiated in Birmingham, Alabama, by Dr. Lori Brown to define the prevalence of breast implant rupture. Dr. Brown, who is on detail to DCEG from the Food and Drug Administration, recently published two reviews: one on breast implant rupture, and the second on the connection between silicone breast implants and autoimmune disease. (Brown, SL; Silverman, BG; Berg, WA. "Rupture of silicone-gel breast implants: Causes, sequelae, and diagnosis," *Lancet* 1997; 350:1531–7; Brown, SL; Langone, JJ; Brinton, LA. "Silicone breast implants and autoimmune disease," *J Am Med Women's Assn* 1998; 53:21–4.) ■

Joanne Dorgan

Occupational Epidemiology Branch

A recent paper by Dr. Patricia Stewart and colleagues describes the development of a new questionnaire with job-specific questions designed to improve the quality of assessment of occupational exposures in community-based studies. The procedures employ task-based and industry-based modules that gather detailed information on materials and equipment, sensory descriptions, engineering controls, and protective equipment. (Stewart, PA; Stewart, WF; Siemiatycki, J; Heineman, EF; Dosemeci, M. "Questionnaires for collecting detailed occupational information for community-based case control studies," *Am Ind Hyg Assoc J* 1998; 58:39–44.)

An extended followup of approximately 15,000 workers at an aircraft maintenance facility revealed associations between exposure to organic solvents and risk of non-Hodgkin's lymphoma and multiple myeloma among men and women. Exposure to solvents and other chemicals also increased the risk of breast cancer among women. (Blair, A; Hartge, P; Stewart, PA; McAdams, M; Lubin, J. "Mortality and cancer incidence of workers at an aircraft maintenance facility exposed to organic solvents and other chemicals: Extended follow-up," *Occup Envir Med* 1998; 55:161–71.)

A recent book from an IARC workshop held in 1996 focuses on methodologic issues associated with incorporating biomarkers into epidemiology investigations of cancer. Dr. Nat Rothman served as one of the editors, and a number of DCEG investigators contributed to individual chapters. ("Application of biomarkers in cancer epidemiology," in *IARC Scientific Publ. No. 142*. Toniolo, P; Boffetta, P; Shuker, DEG; Rothman, N; Hulka, B; Pearce, N, eds. IARC: Lyon, France, 1997.) ■

Aaron Blair

Radiation Epidemiology Branch

Dr. Ethel Gilbert and Dr. Jay Lubin, Biostatistics Branch, served as members of the National Research Council Committee on the Health Risks of Exposure to Radon (BEIR VI). The recently released report concluded that smokers who are exposed to radon appear to be at an even higher risk for lung cancer because the effects of smoking and radon are more powerful when the two factors are combined. Indoor radon contributes to about 12 percent of lung cancer deaths each year in the United States.

Studies of childhood acute lymphoblastic leukemia (ALL) and electromagnetic fields (EMF) have produced three recent publications:

1) **Case-control study of childhood acute lymphoblastic leukemia and residential radon exposure.** In contrast to prior ecologic studies of radon and childhood leukemia, the results from this analytic study provide no evidence for an association between indoor radon exposure and childhood ALL. (Lubin, J; Linet, M; Boice, J; Buckley, J; Conrath, S; Hatch, E; Kleinerman, R; Tarone, R; Wacholder, S; Robison, L. "Case-control study of childhood acute

lymphoblastic leukemia and residential radon exposure," *J Natl Cancer Inst* 1998; 90:294–300.)

2) **Association between childhood acute lymphoblastic leukemia and use of electrical appliances during pregnancy and childhood and residential wire codes.** Increased risks for childhood ALL were associated with several appliances. However, the inconsistency in the dose-response patterns for many appliances, reporting and selection bias, and the lack of an effect for measured 60-hertz magnetic fields or wire codes in the companion study, must be considered before ascribing these associations to exposures from magnetic fields. (Hatch, E; Linet, M; Kleinerman, R; Tarone, R; Severson, R; Hartsock, C; Haines, C; Kaune, E; Friedman, D; Robison, L; Wacholder, S. "Association between childhood acute lymphoblastic leukemia and use of electrical appliances during pregnancy and childhood," *Epidemiology* 1998; 9:234–245.)

3) **Reproducibility and relationship with measured magnetic fields and residential wire codes.** Misclassification of wire code categories was determined not to be a major source of bias in the study of childhood ALL and magnetic field exposure. (Tarone, R; Kaune, W; Linet, M; Hatch, E; Kleinerman, R; Robison, L; Boice, J; Wacholder S. "Residential Wire Codes: Reproducibility and relationship with measured magnetic fields," *Occup Envir Med* 1998; 55:333–339.) ■

NEWS FROM THE TRENCHES

Genetic Epidemiology Branch

Dr. Neil Caporaso was the Chairperson for a special educational session entitled "Molecular Epidemiology: Current Perspectives" at the annual meeting of the American Association for Cancer Research (AACR) in New Orleans in March. The purpose of the session was to encourage interaction among basic, clinical, and population researchers. During the session, Dr. Rashmi Sinha, Nutritional Epidemiology Branch (NEB), spoke on "Transitional Studies: The Link Between the Laboratory and Population Studies"; Dr. Lea Harty, Genetic Epidemiology Branch (GEB), on "The Case-Control Approach to Molecular Epidemiology"; and Dr. Nathaniel Rothman, Occupational Epidemiology Branch (OEB), on "Cohort Studies: Evaluating Exposure, Early Biologic Effects, and Susceptibility."

The Melanoma Consortium was hosted by GEB on June 1 and 2. The meeting included several groups collaborating on family studies of melanoma. Investigators from Australia, Canada, Great Britain, Italy, the Netherlands, Sweden, and the United States attended the meeting. ■

Occupational Epidemiology Branch

Dr. Dalsu Baris chaired a session on neurodegenerative diseases, neurobiological disorders, and electromagnetic field (EMF) exposures at the EMF Science Review Symposium in San Antonio, sponsored by the National Institute of Environmental Health Sciences (NIEHS).

Dr. Ken Cantor and Dr. Mary Ward served on a DHHS subcommittee to identify research and information needs regarding drinking water and health effects. Chaired by Dr. Richard Jackson, Director, National Center for Environmental Health, CDC, the committee included representatives from HHS agencies (NIEHS, NCI, National Institute for Occupational Safety and Health [NIOSH], Indian Health Services, FDA) and other Federal agencies, including EPA and Department of Agriculture. The committee published its recommendations in a report, "Drinking water and human health: The role of the U.S. Department of Health and Human Services."

Dr. Aaron Blair and Dr. Patricia Stewart served as members of an International Agency for Research on Cancer (IARC) Working Group in Lyon, France, to evaluate a number of industrial chemicals for Volume 71 in the series of *IARC Monographs on Evaluation of Carcinogenic Risks to Humans.*

Congratulations to Dr. Michal Freedman, who completed requirements for her Ph.D. in Epidemiology from Johns Hopkins School of Hygiene and Public Health. The title of her dissertation was "A population-based case-control study on the association between nitrates in drinking water and non-Hodgkin's lymphoma."

A new Computer-assisted Personal Interview (CAPI) program has been developed for a case-control study of bladder cancer in Spain. This system, developed by Westat for the Occupational Epidemiology Branch investigatory team led by Drs. Dosemeci, Rothman, and Silverman, incorporates the job-specific modules developed by Dr. Stewart into the CAPI program. This program can be readily modified for other investigations. Contact the OEB if you wish to learn more about the system for your own studies. ■

ADMINISTRATIVE UPDATES

Research Contracts Branch

As a result of a recent legal opinion, NCI staff who have project officer responsibilities with a proposing institution are now precluded from serving on a Technical Evaluation of Proposal committee for the R&D process since this could be viewed as conflict of interest. The "Orange Book" (Section II, A, Part 1: Research and Development, page II–A2) has been changed to reflect this new restriction, as follows: "In addition, NCI staff are prohibited from reviewing a proposal from an institution where he or she has Project Officer responsibilities."

Changes have also taken place within the Research Contracts Branch that will enable the staff to better serve the changing program needs of the National Cancer Institute. The new organization is shown below.

Epidemiology and Support Section
(Previously, Cancer Etiology Contracts Section)
Chief: Beverly L. Wyatt
Deputy Chief: Sharon A. Miller
Divisions Supported: Division of Cancer Epidemiology and Genetics; Division of Clinical Sciences; Division of Basic Sciences; Office of the Director, NCI

Treatment and Biology Section
(Previously, Treatment Contracts Section)
Chief: Nancy E. Coleman
Deputy Chief: Richard Hartmann
Divisions Supported: Division of Cancer Treatment and Diagnosis; Division of Cancer Biology

Prevention, Control and Population Sciences Section
(Previously, Prevention and Control Contracts Section)
Chief: Jeannette J. Johnson
Deputy Chief: Susan Hoffman
Divisions Supported: Division of Cancer Prevention; Division of Cancer Control and Population Sciences

Purchasing and Support Acquisition Section
(Previously, Purchase and Support Contracts Section)
Chief: Todd Cole
Area Supported: Simplified Acquisitions (<$100,000) and Commercial Item Acquisitions (<$5 million) for all of NCI ■

Sharon A. Miller

SPECIAL AWARDS

The following awards were made by Dr. Klausner to staff members at the DCEG Town Meeting in February.

Government Service Longevity Awards
(certificate and pin)

Ms. Denise Duong
Radiation Epidemiology Branch (not pictured)
In recognition of 10 years of service in the Federal Government

Ms. Jennifer Donaldson
Biostatistics Branch
In recognition of 20 years of service in the Federal Government

HHS Quality of Work Life Award
(certificate)

Dr. Elaine Ron
Radiation Epidemiology Branch
For her efforts to improve the overall workplace environment by strengthening communications with employees and for her promotion of communication skills among women scientists of DCEG.

Cowinners of the 1997 DCEG Mentoring Award
(plaque and a $3,000 Special Act Award)

Dr. Shelia Zahm
Occupational Epidemiology Branch
Citation on the Plaque: Dr. Shelia Zahm possesses all the qualities of an outstanding mentor. Her knowledge of epidemiology is exceptional, and she willingly dispenses her wisdom with patience and enthusiasm. Dr. Zahm is always available to discuss projects and answer questions. Her reinforcing and reassuring manner inspires fellows to strive for excellence. Her colleagues learn from her the value of encouraging others and seizing opportunities for challenging and rewarding work. Dr. Zahm is a special role model, and well deserving of the Mentoring Award.

Dr. Dilys Parry
Genetic Epidemiology Branch
Citation on the Plaque: Dr. Dilys Parry has mentored fellows for almost 20 years. She spearheaded NIH's Interinstitute Medical Genetics Training Program and developed NCI's Cancer Genetics and Epidemiology Training Program. For the new NCI Program, Dr. Parry is organizing a series of didactic courses focusing on clinical, molecular, and population genetics that are germane to fellows and other scientists at all levels. She has a genuine interest in the well-being of fellows, and her door is always open for discussions about science, career plans, and life in general. These positive characteristics along with her level-headed and encouraging attitude make Dr. Parry a most deserving recipient of the Mentoring Award.

1997 Outstanding Paper by a Fellow in DCEG
(plaque and $1,000 cash award)

Dr. Lea Harty
Genetic Epidemiology Branch
Dr. Harty received this prestigious award for her paper entitled "Alcohol Dehydrogenase 3 Genotype and Risk of Oral Cavity and Pharyngeal Cancers," which reported risks of oral cancer to be highest among heavy drinkers homozygous for the 1–1 genotype of alcohol dehydrogenase-3 (ADH3). ADH3 is a genotype that appears to rapidly metabolize ethanol to acetaldehyde, for which there is evidence of carcinogenicity in laboratory animals. ■

DCEG PEOPLE IN THE NEWS

Dr. Wong-Ho Chow and **Dr. Debra Silverman,** Occupational Epidemiology Branch (OEB), were accepted into the American Epidemiological Society, a prestigious organization of senior-level epidemiologists.

Ms. Gloria Gridley, Biostatistics Branch, recently received the Distinguished Federal Employees Award from Blue Cross-Blue Shield for her ongoing role in promoting science in the schools and the community. She is a member of the Quantitative Literacy (QC) Committee of the Washington Statistical Society and the Graduate Women in Science's "sisters in science" (SIS) program. Ms. Gridley has been involved in a variety of efforts to promote science, including teaching statistics, mentoring, serving on the Rockville Science and Technology Commission as a mayoral appointee, and judging Fairfax and Montgomery County science fairs. Most recently, Ms. Gridley paired students in the sixth grade with scientist coaches to help them prepare competitive science fair projects to enter the Montgomery County Science Fair, in which one of these students was awarded first prize in zoology.

Dr. Neely Kazerouni, Nutritional Epidemiology Branch, was named as the DCEG representative to the newly formed NIH Predoctoral Fellows Committee.

Dr. Sandra Petralia, OEB, and **Dr. Frank Groves,** Biostatistics Branch, have replaced Dr. Lea Harty, Genetic Epidemiology Branch, and Dr. Mary Ward, OEB, as DCEG representatives to the NIH Fellows Committee.

Dr. Shelia Zahm has been appointed Deputy Director of DCEG. She joined NCI as a Staff Fellow in 1980, and has been Deputy Chief of the Occupational Epidemiology Branch since 1996. Dr. Zahm's research in cancer epidemiology has been focused on detection of high-risk occupational groups and effects of exposure to pesticides and others chemicals, with particular emphasis on the etiology of lymphomas. ■

COMINGS…GOINGS…

Dr. Andrew Bergen, a Fellow in the Human Genetics Program, is working on a review of smoking phenotypes and related factors, and is evaluating various cohorts for a possible genetic study of susceptibility loci associated with nicotine dependence. He is located in EPN / 400 and can be reached at 402–9529.

Dr. Christina Bromley, a Fellow in the Human Genetics Program, is working with Dr. Goldstein on a melanoma data set to evaluate different methodologies to investigate clustering. This effort will help to establish the best approaches to analyze clustering among melanoma families. Dr. Bromley received a Ph.D. from the University of Nebraska. She is located in EPN / 400 and can be reached at 402–9638.

Dr. Naoko Ishibe, a Human Genetics Program Fellow, is studying the characteristics of bronchioalveolar lung carcinoma at the National Naval Medical Center. In particular, she is evaluating how its presentation, risk factors, and outcome differ from adenocarcinoma of the lung. Dr. Ishibe is also participating in a study of chronic lymphocytic leukemia to contrast the epidemiological and clinical features of familial cases with their sporadic counterparts, as well as the pattern and occurrence of cancer in the families. She is located in EPN / 400 and can be reached at 435–3348.

Mr. Dave Kaufman, a Fellow in the Laboratory of Population Genetics (LPG), is working with Dr. Jeff Struewing on *BRCA1* and *BRCA2* mutations in high-risk families, as well as searching for evidence of a third breast cancer gene. Mr. Kaufman is working on a Ph.D. in Genetic Epidemiology at Johns Hopkins University. He is located in EPN / 531 and can be reached at 435–4905.

Ms. Jenny Kelley recently joined the LPG as the Technical Laboratory Manager. She comes to DCEG from The Institute for Genomic Research (TIGR), where she set up high-throughput automated DNA sequencing, organized the laboratory, hired and trained the staff, and conducted research and development. In LPG, she will organize the

laboratory and train the staff, as well as serve as a technical resource to investigators developing their own research activities. In addition, Ms. Kelley will be a valuable resource for NCI's Advanced Technology Center, which will perform high-throughput DNA genotyping and sequencing. Ms. Kelley is located in Building 9 and can be reached at 435–8954.

Dr. Kai-Li Liaw, after 6 years at the NCI, said farewell to the Environmental Epidemiology Branch and accepted an Assistant Professorship in the Department of Epidemiology at the University of Pittsburgh.

Mr. Roberto Minutillo, who recently joined the ARC as an Administrative Officer, is an Administrative Career Development (ACD) Intern with the NCI and will be in this position for 9 months. Mr. Minutillo began his ACD internship with the Grants Administration Branch and the Research Contracts Branch. Before ACD, Mr. Minutillo was a Purchasing Agent in the Clinical Center. He is located at EPN / 539 and can be reached at 594–7210.

Dr. Dirk Moore, who is from the Statistics Department at Temple University, is spending a 6-month sabbatical in the Biostatistical Branch. He has degrees in Mathematics, Biostatistics, and Biology. Dr. Moore spent a year in Japan at RERF and 5 years in an adjunct position with the Fox Chase Cancer Center. In the Biostatistics Branch, he is working on methods to estimate the cumulative risk of breast cancer by a given age for carriers and noncarriers of mutations in the *BRCA1* and *BRCA2* genes. The estimates are based on the kin-cohort design used by DCEG scientists to study cancer risk and mutation carriers in Ashkenazi Jews. Dr. Moore is located in EPN / 431 and can be reached at 496–4155.

Dr. Andrew Olshan, an Associate Professor of Epidemiology at the University of North Carolina, has joined the Occupational Epidemiology Branch for a 6-month sabbatical. Dr. Olshan is interested in methods of exposure assessment for community-based studies, childhood cancer, and gene-environment interactions

Dr. Susan Sieber has been appointed Associate Director for Special Projects in the Office of the Director, NCI. In this new position, Dr. Sieber will be responsible for assisting Dr. Klausner in developing policy related to the intramural and extramural functions of NCI, serving as a liaison between the Director's office and advisory groups, and coordinating NCI activities in a variety of areas. Dr. Sieber was Deputy Director of DCEG.

Mr. Mike Stevens, a student at Montgomery College, has joined the Environmental Epidemiology Branch through the STEP program and will be providing administrative and clerical support to the Branch. He is located at EPN / 443 and can be reached at 496–1693.

Dr. Louise Wideroff (Environmental Epidemiology Branch) and **Dr. Andrew Freedman** (Genetic Epidemiology Branch) recently joined the Applied Research Branch in the Division of Cancer Control and Population Sciences, NCI.

Dr. Tamara Zemlo has joined the Environmental Epidemiology Branch through the Division of Cancer Prevention Fellowship Program. She is working with Dr. Mark Schiffman on determining if HPV positivity predicts recurrence and progression of cervical cancer precursor lesions. She received a Ph.D. from the University of Wisconsin, writing her dissertation on cellular transformation by the human papillomavirus, and an M.P.H. from the Harvard School of Public Health. Dr. Zemlo is located at EPN / 443 and can be reached at 435–3976. ■

OBITUARY

The Genetic Epidemiology Branch recently lost a close collaborator of 20 years, Dr. Wallace H. Clark, Jr., who died in November 1997. At the time of his death, Dr. Clark was a distinguished pathologist affiliated with Beth Israel Hospital / Harvard Medical School and the Pigmented Lesion Study Group at the University of Pennsylvania. He was dedicated to the study of the neoplastic process, with a particular emphasis on melanoma, and developed the now-standard microstaging system for melanoma lesions (the Clark Classification System). He was the coauthor of over 135 scientific articles, 2 of which were recently published: "Problems with lesions related to the development of malignant melanoma: Common nevi, dysplastic nevi, malignant melanoma in situ, and radical growth phase malignant melanoma" (Clark, WH, Jr; Tucker, MA. *Hum Pathol* 1998; 29[1]:8–14), and "Atypical melanocytic nevi of the genital type with a discussion of reciprocal parenchymal-stromal interactions in the biology of neoplasia" (Clark, WH, Jr; Hood, AF; Tucker, MA; Jampel, RM. *Hum Pathol* 1998; 29[1] Suppl 1: S1–S24). His keen insight, enthusiasm for science, and indomitable good nature will be missed. ■

CALENDAR OF EVENTS

Following is a schedule of upcoming events of particular interest to DCEG.

Date	*Meeting*
June 9–10	General Motors Cancer Research Foundation Conference
June 18	Senior Advisory Group 1–4 p.m., EPN / H
June 22	DCEG Women Scientists Brown Bag Lunch Noon, EPN / H
July 9	Senior Advisory Group 1–4 p.m., EPN / H
July 13	Board of Scientific Counselors–A
July 23	Senior Advisory Group Retreat Glenview Mansion, Rockville
August 13	Senior Advisory Group 1–4 p.m., EPN / H
September 9–11	National Cancer Advisory Board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