DCEG LINKAGE

Division of Cancer Epidemiology & Genetics
National Cancer Institute
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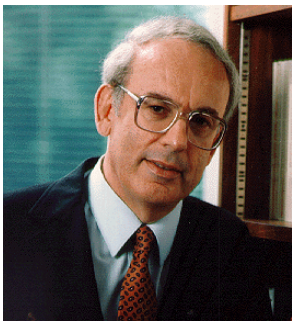
Director's Page

The DCEG Challenge



Epidemiology is often described as opportunistic because it takes advantage of natural experiments and exciting opportunities as they arise, so that long-term planning has to be able to accommodate unanticipated challenges. Nevertheless, it is important that the Division engage in a planning process to identify the most compelling scientific and public health issues, particularly those that can be addressed most efficiently in our intramural research program. In the NCI's Fiscal Year 1999 Bypass Budget Proposal, entitled *The Nation's Investment in Cancer Research*, Dr. Klausner describes a series of "extraordinary opportunities" for immediate investment in cancer research. First and foremost is the area of cancer genetics, which includes a general outline of objectives, opportunities, and strategies for research in the coming years.

The Division is responding to this investment opportunity in cancer genetics by placing greater emphasis on genetic and molecular epidemiology to identify susceptibility genes and gene-environment interactions for various cancers. Toward this end, we are fortunate that Ken Buetow (see profile on p. 4) will join us to head our new Laboratory of Population Genetics. In addition, efforts are underway to recruit a chief for the new Clinical Genetics Branch, who will direct efforts to expedite clinical applications of the unprecedented discoveries being made in molecular genetics. Another effort to expand the talent pool in this area involves our fellowship programs in genetics and epidemiology, which have been invigorated by the efforts of Dilys Parry, Trisha Hartge, Sholom Wacholder, Joanne Colt and others.

As we strengthen our efforts in genetic and molecular epidemiology, the Division and Institute must develop the epidemiologic and laboratory resources to sustain our research programs. Ken Buetow is taking the lead to establish an NCI core facility for high throughput genotyping and sequencing, while Neil Caporaso is chairing an NCI-wide working group to create a biospecimen repository and processing laboratory to support our population-based studies. These resources will be particularly crucial to our increased efforts in nutritional epidemiology and hormonal carcinogenesis as greater attention is given to genetic and biochemical probes.

At the recent DCEG Retreat, Program Directors and Branch Chiefs presented overviews of the scientific areas they plan to pursue in expanding our understanding of cancer etiology. The discussion of their "research visions" was valuable in identifying promising opportunities and in thinking about future priorities. It was recognized that important opportunities often arise quickly and that flexibility is needed to respond rapidly and efficiently to them. Now that the Program Directors and Branch Chiefs have had some time since the Retreat to reflect on their research visions, as well as to discuss them with their senior staff members, I thought it would be useful to present them in *Linkage*, starting in this issue with those of Louise Brinton, Mitchell Gail, and Jim Goedert. Since our Division thrives on collaboration, interaction, and debate, one might expect that over time their research visions may overlap and coalesce in ways that will further shape our overall priorities.

In a section of the Bypass Budget Proposal titled "NCI's Challenge," Dr. Klausner indicates that "we are in golden age of discovery, one unique in human history." It is clear that our Division has a critical role to play in accelerating

and broadening the process of discovery in cancer causation and its application to prevention, particularly through interdisciplinary strategies that integrate epidemiologic with laboratory and clinical approaches. The opportunities for molecular epidemiology are particularly exciting in view of the explosive developments in cancer biology and the interplay of ideas as scientists with different backgrounds join forces in the discovery process. The strength of DCEG is derived not only from its comprehensive, balanced, and collaborative approach to cancer etiology, but also from the diversity of individual perspectives that provide multiple points of entry into the study of cancer etiology, including gene-environment interactions. Molecular epidemiology is an approach whose time has come, and if we can tap the enormous potential of other groups at NCI and NIH for interdisciplinary research in this area, the advances in knowledge will be spectacular.
.....by Joseph Fraumeni

A MESSAGE FROM THE OFFICE OF DIVISION OPERATIONS AND ANALYSIS

DCEG Intramural Research Award

The DCEG Intramural Research Award (IRA) is a new competitive funding mechanism to encourage exciting interdisciplinary projects that are innovative and cross the usual organizational boundaries. IRA recipients are recognized for their creative ideas and scientific skills in advancing the goals of the National Cancer Institute.

Features of the IRA program include the following:

- Only Principal Investigators (PIs) are eligible to receive an IRA, although scientific collaborators may include non-PIs;
- Priority will be given to collaborative projects that are innovative and have potential for significant scientific or public health impact, including development of resources to facilitate population-based research (e.g., creation of a novel database or research model);
- Each IRA will be up to $75,000 per fiscal year and renewable for up to three years (subject to availability of funds), though priority will be given to pilot studies and other projects that can be completed within one year;
- Unified applications are encouraged from investigators in the different scientific disciplines needed to carry out the objectives of a project;
- The amount of the IRA will not be considered as part of a PI's base budget, and therefore will not be subject to evaluation during site visits or other resource reviews;
- Research accomplishments resulting from IRAs may be used by a PI to request a base budget increase during resource reviews, which then becomes subject to normal Board of Scientific Counselors (BSC) review;
- IRAs from other intramural divisions may be used in conjunction with an award from DCEG.

Evaluation factors used to assess the merit of an IRA application include the following:

- Potential for significant scientific or public health impact;
- Innovative aspects of the approach or method;
- Interdisciplinary nature of the project, especially in utilizing collaborative links with other NCI divisions;
- Ability to achieve the objectives within the proposed time frame and resources;
- Programmatic relevance to the mission of DCEG.

If you are interested in submitting an application for an IRA, your write-up should be limited to five single spaced pages. An additional page should detail your budget requirements, and extra pages are allowed for tables, figures and references. The scientific section of your application should be divided into the following parts:

- Specific objectives, including programmatic relevance to DCEG's mission;
- Background and applicable preliminary data;
- Proposed research, including approach;
- Contribution of each collaborator.

Although applications are due March 1, PIs may request their funding to commence in FY 99 if there is inadequate time to initiate the project in this fiscal year. Applications will be reviewed by a joint intramural/extramural committee, and IRA recipients will be announced in late March or early April. Three hard copies or an electronic version (preferably in WordPerfect) should be submitted to:

Dr. James Sontag
Chief, Office of Division Operations
and Analysis
Division of Cancer Epidemiology
and Genetics
Executive Plaza North, Room 543
sontagj@epndce.nci.nih.gov

Please contact Dr. Sontag concerning questions about the IRA.

DCEG Mentoring Award

The Division has created a new annual Mentoring Award to honor the scientist deemed to be the most outstanding mentor by the DCEG fellows. Nomination and selection of the candidates may be made by any fellow who worked at any time during the year in the Division. Any DCEG scientist (tenured investigator, tenure-track investigator, or staff scientist) who interacts with a fellow in any type of mentoring capacity is eligible to receive the award. A scientist does not have to be designated as an "official mentor" to be eligible.

The selection of the Mentoring Award winner involves the following:

- The award process is overseen by the Ms. Joanne Colt, the DCEG Fellowship Coordinator;
- Nominations are submitted to Ms. Colt in November and the winner is selected in December;
- Each fellow may nominate two DCEG scientists for the award, with each nomination supported by a written rationale.
- The nomination rationales are placed on file in Ms. Colt's office, where fellows may read them and cast their ballot for their choice of the outstanding mentor.
- Votes are tallied by Ms. Colt.

A plaque and a $3,000 Special Act Award is given to the winner of the Mentoring Award. The 1997 winner will be announced at the NCI Director's Town Meeting for DCEG on January 26, which starts at 2:00 pm in EPN/H.

Award for the Outstanding Research Paper of the Year by a Fellow

The Outstanding Research Paper of the Year by a DCEG Fellow is another annual award created by the Division in 1997. This award honors a postdoctoral or predoctoral fellow for the best research paper published during the past calendar year. The winning paper is singled out based on its impact, innovation, and clarity of thought and language. Eligibility criteria are:

- The fellow must be the lead author;
- The paper must be based on research conducted while a fellow in NCI;
- The paper must be based on research supported by DCEG; and
- The paper must appear in print during the past year.

The process for choosing the outstanding paper starts with the Directors of the Division and Programs, who review the publications submitted by the DCEG Branch Chiefs and make an initial selection of the top candidates. These papers are provided to the DCEG Senior Advisory Group (SAG) members, who may make additional nominations. The papers are discussed at the February SAG meeting, and the most outstanding paper is selected by the members in a secret ballot. The winner receives a plaque and a travel award of $3,000.

.....by Jim Sontag

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PROFILE

Kenneth H. Buetow, Ph.D.

The scientist recruited to be Chief of DCEG's new Laboratory and Population Genetics Branch is a man who truly enjoys his work. Dr. Buetow has managed to meld his passion for science with his love for computers. The laboratory component lets him work with specifics and get tangible results; the analytic part satiates his desire to understand the quantitative underpinning of biology; and the computer affords him the opportunity to create programs that also combine the other two disciplines. "I am fortunate to be working at what I love, and I'll probably keep doing all of it even when I retire," says Dr. Buetow. "I can't imagine doing anything else."

Dr. Buetow says he was never directed toward science. In fact, his parents thought he would become an architect, because he was always building things. The world of science came alive for him in grade school. "I especially remember my sixth grade science teacher whose enthusiasm for science and for teaching was infectious," says Dr. Buetow. "His science projects and demonstrations were both informative and fun, and I was completely hooked." Science has been such a rewarding experience for Dr. Buetow that he often shares his experience with high school and college students through lectures, by conducting laboratory tours, and permitting students to perform research internships in his shop. These actions are derived from his strong belief that we should give something back to the community that enabled us to succeed.

Dr. Buetow will come to NCI from the Fox Chase Cancer Center, where cancer biology and gene-mapping have been among his areas of expertise. He received a B.A. in biology from Indiana University, and his M.S. and Ph.D. in human genetics, with an emphasis on biostatistics, from the University of Pittsburgh.

As an undergraduate, Dr. Buetow pursued life sciences but found them undisciplined. He enjoyed the quantitative mechanical nature of the physical sciences, but found them vacuous and non-stimulating. He says he couldn't get excited about filling test tubes and watching chemicals change colors. Physics experiments were never very stimulating, and astronomic physics seemed dry. Dr. Buetow says that it was a struggle to discover his scientific bent until he took a genetics course that opened a new world. "It was like an epiphany, he says, "because suddenly there was biology with the rigor of physics and chemistry and an instructor who made the course come alive." Dr. Buetow paraphrases his professor's definition of genetics as "the algebra of life. It is the underlying mechanics through which life occurs." With genetics, he had a synthesis of his interest in mathematics, quantitative work, and biology.

However, even the best plans go awry. For Dr. Buetow, it was almost a disaster. His organic chemistry professor almost single-handedly rid the world of a budding scientist. The purpose of the class, says Dr. Buetow, was to weed out casual pre-med students. It also eliminated people who were interested and quite capable but devastated by this experience. The rigors of the class were so hard and inflexible that often the mean of an exam was 20%. "It was a completely demoralizing experience," said Dr. Buetow. He thought if this was what science was about, he wasn't going to be a part of it. He changed his focus and explored other areas like liberal arts and political science. On a whole, this exploration was a positive experience for Dr. Buetow, which he feels has served him quite well through the years.

When he's not in the lab or on the computer, Dr. Buetow spends as much time as possible with his family. He and his wife, Dr. Katherine McGlynn, an epidemiologist at Fox Chase, are the parents of two daughters, Claire (8) and Emily (5). Although once a long-distance runner, he doesn't have much time for it now. His wife is the serious runner in the family and has participated in several marathons.

Recently, ***Linkage*** met with Dr. Buetow in his office at EPN. In the interview, he comments on the role of his new laboratory in DCEG, and gives some advice to new scientists.

Linkage: What will your role and that of your staff be, and how will it enhance DCEG's mission?

Buetow: Human genetics and human genomics will be my main focus, and my key role is to bring in-house the capacity to do laboratory-based investigations in this area. There have been outstanding programs at NCI for years, and much of what we know about cancer genetics has come out of DCEG. I will be bringing people into the fold of this outstanding collection of people in genetics and epidemiology who will be doing hands-on laboratory-based evaluations in genetics and genomics. Why do some people develop cancer and other people don't is a very motivating question for me. The insight and interest I bring to this question is the evaluation of the role of one's genetic constitution in determining risks. The underlying theme of my program is to see how we can use today's powerful tools in molecular genetics to understand how people are different in their overall genetic constitution, more particular in their response to their environment and their susceptibility to disease.

There are multiple facets to the program. Because DCEG is on the brave new frontier of human genetics, we will be required to continue to expand the foundation of basic genomics. Despite what might be the perception, very little is known about the genetic architecture of human populations. The underlying patterns of variability in populations need to be aggressively investigated. One of the most exciting challenges is that it's estimated that approximately one in one thousand nucleotides varies in the DNA that I got from my mom versus the DNA strand that I got from my dad. Just within my genetic constitution that translates out to a million differences in my genetic code. I feel that knowing about this kind of diversity might aid in modulating disease risks as well as suggesting some of the exciting new areas that I think genetics will be stepping into in the future. For example, there are studies now that are investigating the response to drugs based on our genetic constitution. We are all created equal, but we all have substantial differences, which if ignored by the medical community could result in medical policies and practices that might not be maximally beneficial to each individual. I feel that if we know more about a person's genetic constitution, it will help in tailoring our whole view of medicine and biology.

Linkage: Does your new mission differ substantially from that at Fox Chase?

Buetow: The major difference is in scale. Conceptually, almost all the components in my research program will be the same. The main exceptions will be the establishment of two core facilities to support the broader NCI community. One facility will conduct large-scale sequencing and the other will do high throughput genotyping.

High throughput genotyping will give DCEG the capacity to conduct large population-based studies on site, which will enable scientists to do genetic characterizations in-house. The advantage is that the specific investigations can be dynamically tailored around the changing research interests of the investigators.

Large-scale sequencing is an increasingly important component of any genetics research program, because it has become clear that one of the primary commodities in genetic investigations is sequence. In my research programs, the principal interest is the study of the genetic basis of gene-environment interactions in producing risks for the common cancers. In my genomics work, I will be developing reagents for high-resolution genetic analysis and developing the statistical and technical tools required to analyze the laboratory outcomes.

Linkage: What do you feel is your greatest scientific accomplishment to date?

Buetow: I feel that my greatest accomplishment, recognized by the scientific community, is the production and distribution of human genetic maps. But I hope that our work on primary liver cancer will be interpreted in the future as an important body of work. We were one of the first groups to show an interaction between a well-defined environmental exposure and genetic constitution in determining risk. We showed that in primary liver cancer, risk associated with chronic hepatitis B virus and aflatoxin B-1 exposure is modified by an individual variation in genes that metabolize the carcinogens.

The relative risk for developing liver cancer from hepatitis-B infection is approximately 10. The genetic factor increased risk three-fold. When the genetic factor and hepatitis-B infection are combined in an area where aflatoxin B-1 exposure is ubiquitous, there was a greater than 80-fold increase in risk.

Linkage: What advice would you give new scientists?

Buetow: I advise new scientists to learn as much as they can and be sure to develop good computer skills. The problems will become more complex in the next five to ten years, and computers will be increasingly more important in our ability to assemble the data that we need as scientists. Computer skills will be even more critical in manipulating large quantities of information. With the explosion of biomedical research information engulfing us, anyone with computer skills will be at a strategic advantage.

I would also warn young scientists against over specializing, even when they are being pressured by their schools and recruiting institutions. The key for me has been to be able to borrow from the many different academic skills for my research work. I also think we will soon begin to see a renaissance of people who are more generalists.

Linkage: What profession would you have pursued if not science and why?

***Buetow*:** During some frustrating times in my graduate years, when I was looking at my small stipend and dealing with a mentor whose philosophy was "to make the scientist, you have to break the scientist," I toyed with the idea of being a computer programmer. Some of my colleagues with similar educational backgrounds were making significantly more money, working regular hours, and having a real life. I actually do computer programming now, which is a key component of my work in informatics.

.....by Pat Evans

RESEARCH VISIONS

The NCI is placing greater emphasis on long-term planning of research initiatives and the resources needed for its support. To ensure that DCEG is actively involved in the planning process, it is essential that each Branch have a research vision whose elements mesh with the Institute's strategic plans. In this issue, the research visions of three of the Division's Branches are summarized below.

Biostatistics Branch

The vision of the Biostatistics Branch is to be an outstanding applied statistics and descriptive epidemiology unit capable of contributing new information on cancer etiology and responding to the scientific priorities of DCEG by (1) providing expert consultation and active collaboration on study design and analysis; (2) leading selected epidemiologic studies; and (3) developing innovative statistical, computational and other needed methods.

Understanding the scientific opportunities and directions in cancer research is the beginning of a successful DCEG program in biostatistics. Such awareness arises from service on committees, such as the Committee for Technical Evaluation of Proposals; from participation in scientific working groups and seminars; and from consultation and active collaboration on major projects throughout DCEG. Some examples of major collaborative projects in which the Branch staff have recently played include: a study of the risks of exposure to benzene in China (with OEB); a study of the penetrance of the BRCA1 and BRCA2 genes predisposing to breast cancer (with GEB); studies of the prognosis of hemophiliacs infected with HIV (with VEB); combined analyses of the risk of lung cancer from exposure to radon in underground miners (with REB); the design and conduct of the Agricultural Health Study (with OEB); studies of the reliability of hormone assays (with NEB); and a variety of epidemiologic studies of breast cancer (with EEB). These collaborations require a full range of scientific involvement, including assessment of feasibility, protocol design, monitoring study conduct, analysis and interpretation, and writing a manuscript for the

scientific literature. Biostatisticians offer insights that add immensely to the value of a study, such as the work that shows that one could estimate the penetrance of BRCA1/BRCA2 mutations by determining the medical histories of first-degree relatives of volunteers who agreed to be genotyped.

Such consultations and collaborations also motivate independent methodological and epidemiologic research led by Branch scientists. For example, we are now evaluating the statistical and practical advantages and disadvantages of several designs for estimating the penetrance of identified mutations. The effect of measurement error on the design and interpretation of etiologic studies has been a long-term research theme in the Branch, and recent work concerns the effects of measurement error on detecting gene-environment interactions. Other methodologic research growing out of program needs includes: methods of analysis of case-control studies in which controls are selected by cluster sampling; methods to analyze descriptive data, such as age-period-cohort analyses, and to identify cancers with large geographic variability; and development of data resources such as record-linkage systems to permit studies relating medical conditions or treatments to the subsequent risk of cancer. The ability and resources to conduct methodologic research enable Branch scientists to identify and resolve non-standard methodologic problems in epidemiologic research and to introduce improved methods through consultation and collaboration.

Branch staff members also lead a number of epidemiologic studies. A geographic atlas of U.S. cancer mortality rates from 1970 to 1994 is nearing completion. Analyses of age-specific trends in HIV infection rates are underway, based on AIDS incidence data as well as age-specific rates of progression from HIV infection to AIDS. Several staff members are leading gastric cancer projects in China, including studies to determine whether baseline micronutrient levels are associated with increased risk of gastric cancer and studies to determine whether genetic polymorphisms or somatic mutations are predictive of rates of transition among precancerous states for gastric cancer. An intervention trial is under way in Shandong Province to determine whether treatment for *Helicobacter pylori*, vitamin supplements, or an extract of garlic can retard the progression of precancerous gastric lesions. Building on earlier collaborative work with EEB and GEB, we are developing a model for predicting a woman's risk of breast cancer that incorporates mammographic density as well as other risk factors.

To work effectively in the dynamic and diverse scientific environment of DCEG, our investigators must have a broad range of expertise and be able to adapt to meet new challenges. Additional staff are needed to support the many consultative and collaborative projects in descriptive, analytical, and molecular epidemiology and to encourage the development and integration of new methodologic approaches to interpreting such data. Additional staff are also needed to strengthen capabilities in statistical genetics, especially as applied to population studies.

.....by Mitchell Gail

Environmental Epidemiology Branch

A major focus of the Environmental Epidemiology Branch's research vision is on the etiology of breast cancer. This is an exciting time for breast cancer research, given recent molecular advances. The focus also complements other related ongoing NCI activities, including the Breast Cancer Task Force, the Breast Cancer Progress Review Group, and the recently formulated Breast Cancer Think Tank.

Probably the most exciting opportunities lie in evaluating gene-environment interactions, but much of the ongoing research by individual investigators is hampered by small sample size. Prior to undertaking studies of gene-environment interactions, it is important that close attention be given to statistical considerations. Fortunately, our Branch is in a position, with several ongoing investigations, to have the power to assess the role of a number of genetic mechanisms that may be involved in modulating environmental exposures. We hope that by focusing on both hormone and carcinogen metabolizing enzymes, we might advance our knowledge of several controversial and complex exposures, including exogenous

hormones and environmental contaminants.

Another major area that the Branch wants to emphasize in future breast cancer research relates to gaining a better understanding of biologic mechanisms. Previous investigations have mostly considered breast cancer as a single disease entity, but we feel that much can be learned by identifying more homogeneous and etiologically distinct subsets, based on histology or clinical and biochemical markers. A better understanding of the natural history of the disease is also essential, and studies need to focus on early disease markers. Our earlier work on mammographic densities appears particularly promising for future endeavors. We also hope to expand our studies of endogenous hormones to these early disease states.

Since only a limited proportion of breast cancer is explained by identified risk factors, it will be a challenge to identify promising areas for further exploration. Much of that work in the future will involve close collaboration with laboratory investigators. Some of this research will involve further assessment of well-established risk factors, but other investigations will need to focus on more recently elaborated exposures that may be predictive of risk. For instance, a number of us recently participated in a workshop on physical activity sponsored by the National Action Plan on Breast Cancer, and a number of new research ideas emerged, which can be pursued for breast as well as other cancers.
.....by Louise Brinton

Viral Epidemiology Branch

Viruses are transmissible genes that, like those in humans, have rates and determinants of prevalence, penetrance, and phenotypic expression. Also like human genes, viruses interact with other genes through direct and indirect mechanisms to alter cellular functioning. The Viral Epidemiology Branch applies laboratory techniques and appropriate epidemiologic and statistical methods to all types of field studies to understand the transmission and natural history of cancer- associated viral infections.

As with carcinogenic exposures generally, most infected persons do not develop malignancy. Our perspective usually begins with the virus, largely because the exposure can be well defined and well quantified. The Branch utilizes not only conventional and investigational antibody serology, but increasingly the polymerase chain reaction (PCR) and related molecular methods to unequivocally define and quantify infection with one or more of these viruses, including HTLV-I, HIV-1, HCV, HPV, and HHV8. Most of this work is conducted at the Frederick Cancer Research and Development Center by our dedicated laboratory, the Human Retrovirus Section of the AIDS Vaccine Program.

Our primary focus is on those malignancies (adult T-cell leukemia, non-Hodgkin's lymphoma, Kaposi's sarcoma, cervical and anal cancers, and hepatocellular carcinoma) that have been linked to infectious agents. Pilot studies of other neoplasms may be undertaken, often when an animal virus is known to have carcinogenic activity. Laboratory, clinical, and questionnaire data are analyzed to test specific hypotheses regarding viral transmission and postulated outcomes, including cancer, other diseases, or complete recovery from the infection. Age, therapeutic and recreational drugs, infections with multiple viruses or other pathogens, and occupational or other environmental exposures may all be important. In addition to viruses, host immunity and genetics, especially human leukocyte antigens, chemokines, and chemokine receptors, have become essential components of most studies in the Branch. We look forward to continuing and expanding our collaborations with our many colleagues within and outside of DCEG.
.....by James Goedert

SCIENTIFIC HIGHLIGHTS

In recent months, DCEG scientists have reported a variety of important findings, some of which are summarized below.

Genetics Epidemiology Branch

The findings of a multi-institution study to investigate the risk of developing second primary cancers (other than small-cell lung carcinoma) among survivors of small-cell lung cancer suggest that they should stop smoking and consider entering trials of secondary chemoprevention, because of their substantially increased risk of

subsequent malignancies. The study, designed by the Genetic Epidemiology Branch, used demographic, smoking, and treatment information from the medical records of 611 patients who had been cancer free for more than two years after therapy for histologically proven small-cell lung cancer. It was found that relative to the general population, the risk among these patients of all cancers (mostly non-small-cell cancers of the lung) was increased 3.5-fold. Second lung cancer risk was increased 13-fold among those who received chest irradiation in comparison to a 7-fold increase among nonirradiated patients. It was higher in those who continued smoking, with evidence of an interaction between chest irradiation and continued smoking (relative risk=21). Patients treated with various forms of combination chemotherapy had comparable increases in risk (9.4-to 13-fold, overall), except for a 19-fold risk increase among those treated with alkylating agents who continued smoking. (*Tucker MA, Murray N, Shaw EG, Ettinger DS, Mabry M, Huber MH, Feld R, Shepherd FA, Johnson DH, Grant SC, Aisner J, Johnson BE. Second primary cancers related to smoking and Ttreatment of small-cell lung cancer. JNCI, 89:1782-1788, 1997*).

.....by Pat Evans

Occupational Epidemiology Branch

Considerable attention has been given to the weak estrogenic effect of DDT and its metabolite, DDE, as possible risk factors for breast cancer. A recent collaboration with the National Institute of Public Health in Mexico found no association between serum levels of this organic chlorine pesticide and risk of breast cancer, adding to the growing evidence that these chemicals do not play a role in the development of breast cancer in humans. (*Lopez-Carrillo L, Blair A, Lopez-Cervantes M, Cebrian M, Rueda C, Reyes R, Mohar A, Bravo J. Dichlorodiphenyltrichloroethane serum levels and breast cancer risks: A case-control study from Mexico. Cancer Res, 57:3728-3732, 1997).*

In a study of bladder cancer in Washington County, Maryland, the relative risk rose among smokers with increased duration of use of drinking water from chlorinated surface sources. The restriction of this effect to smokers suggests that smoking may modify a possible effect of chlorinated surface water on the risk of bladder cancer. (*Freedman DM, Cantor KP, Lee NL, Chen L-S, Lei H-H, Ruhl CE, Wang SS. Bladder cancer and drinking water: A population-based case-control study in Washington County, Maryland (United States). Cancer Causes Control, 8:738-744, 1997).*

.....by Aaron Blair

Radiation Epidemiology Branch

Residential Magnetic Field Exposures and Childhood Acute Lymphoblastic Leukemia

In collaboration with the Children's Cancer Group, we recently reported results from a study of residential exposure to magnetic fields from nearby power lines in the current and former homes of 638 children with acute lymphoblastic leukemia (ALL) compared to 620 control children residing in nine midwestern and mid-Atlantic states The risk of childhood ALL was not linked to summary time-weighted average residential magnetic-field levels based on 24-hour measurements in each child's bedroom, 30-second measurements in four other rooms, and a 30-second measurement immediately outside the front door. In addition, the risk of ALL was not increased among children whose main residence was in the highest wire-code category (a surrogate indicator of residential magnetic-field level exposure, based on standardized visual assessments of the distance and configuration of nearby power lines). These results provide little evidence that living in homes characterized by high measured time-weighted average fields or by the highest wire-code category increases the risk of childhood leukemia (*Linet MS, Hatch EE, Kleinerman RA, Robison LL, Kaune WT, Friedman DR, Severson RK, Haines CM, Hartsock CT, Niwa S, Wacholder S, Tarone RE. Residential exposure to magnetic fields and acute lymphoblastic leukemia in children. N Engl J Med, 337:1-7, 1997*).

Residential Radon Exposures and Childhood Acute Lymphoblastic Leukemia

Some ecologic analyses have shown significant positive correlations between mean indoor radon concentrations and risk of childhood leukemia. As part of the comprehensive case-control study of childhood acute lymphoblastic leukemia (ALL) described above, measurements were taken of radon levels in the childrens' bedrooms and the family rooms of past homes of study subjects to investigate the association between risk of

childhood ALL and exposure to radon and its progeny. The mean radon concentration within the exposure assessment period was lower for cases than controls (67.3 versus 77.7 becquerels per cubic meter). For categories <37, 37-73, 74-147, and 148 or greater becquerels per cubic meter (corresponding to categories <1, 1-1.9, 2-3.9, and 4 pico-curies or greater per liter), odds ratios were 1.0, 1.2, 0.8, and 1.0, respectively, based on matched case-control pairs (281 cases vs. 281 controls) and similar to results from an unmatched analysis (505 cases vs. 443 controls). There was no association between ALL risk and radon levels within subgroups defined by categories of age, gender, birth order, birth weight, family income, parental age at the subject's birth, parental occupation, parental smoking habits or type of residence. Radon also was not associated with increased risk of childhood ALL based on the measurements taken in the homes where mothers resided when pregnant with the subjects, nor when a two-year exposure lag interval was assumed. (*Lubin JH, Linet MS, Boice JD Jr., Buckely J, Conrath SM, Hatch E, Kleinerman RA, Robison L, Tarone RE, Wacholder S.: A case-control study of childhood acute lymphoblastic leukemia and residential radon exposure. JNCI. in press).*

Risk of Second Malignant Neoplasms Among Long-term Survivors of Testicular Cancer

Few studies have quantified the risk of second cancers following testicular cancer among large numbers of long-term survivors, taking into account both histologic type of initial tumor and primary therapy. Among a cohort of 28,843 one-year survivors of testicular cancer, identified within 16 population-based tumor registries in North America and Europe, there were over 3,300 testicular cancer patients who had survived more than 20 years. Second cancers were reported in 1,406 subjects (observed-to-expected ratio (O/E) = 1.43, 95% confidence interval 1.36-1.51), with significant excesses noted for acute lymphoblastic leukemia (O/E = 5.20), acute nonlymphocytic leukemia (O/E = 3.07), melanoma (O/E = 1.69), non-Hodgkin's lymphoma (O/E = 1.88), and cancers of the stomach (O/E = 1.95), colon (O/E = 1.27), rectum (O/E = 1.41), pancreas (O/E = 2.21), prostate (O/E = 1.26), kidney (O/E = 1.50), bladder (O/E = 2.02), thyroid (O/E = 2.92) and connective tissue (O/E = 3.16). Overall risk was similar following seminomas (O/E = 1.42) and nonseminomatous tumors (O/E = 1.50). Risk of solid tumors increased with time since testicular cancer diagnosis and reached 1.54 (O/E = 369) among 20-year survivors (P trend 0.00002). Secondary leukemia was correlated with both radiotherapy and chemotherapy, while excess cancers of the stomach, bladder, and possibly pancreas were associated mainly with prior radiotherapy. Men with testicular cancer continue to be at significantly elevated risk of second malignant neoplasms for over two decades following initial diagnosis. Patterns of excess second cancers suggest that several factors may be involved, although the precise role of treatment, natural history, diagnostic surveillance and other influences is yet to be clarified. (*Travis LB, Curtis RE, Storm H, Hall P, Holowaty E, Van Leeuwen FE, Kohler BA, Pukkala E, Lynch CF, Andersson M, Bergfeldt K, Clarke EA, Wiklund T, Stoter G, Gospodarowicz M, Sturgeon J, Fraumeni JF Jr., Boice JD Jr. Risk of second malignant neoplasms among longterm survivors of testicular cancer. JNCI, 89:1429-39, 1997).*

.....by Elaine Ron

NEWS FROM THE TRENCHES

Genetic Epidemiology Branch

The Human Genetics Program (HGP) is offering a series of lectures on cancer genetics, which began on Tuesday, January 27. The series will continue with weekly lectures through May. Coordinated by Dr. Dilys Parry, the lectures are designed for those with little formal knowledge of genetics. The tentative lecture outline was announced on the DCEG ListServe on December 20. Registration is now closed. If you are interested in being placed on a waiting list and have not already registered, please send an e-mail to Dr. Parry at *parryd@epndce.nci.nih.gov*. Include your name, division, institute, and telephone number. Audiotapes of the lectures will be made available by contacting Ms. Sandra Coopersmith at 496-4947.

.....by Dilys Parry

Nutritional Epidemiology Branch

Two papers written by Dr. Rashmi Sinha and collaborators on heterocyclic amine concentrations in meats cooked by different methods have been accepted by the Journal of *Food and Chemical Toxicology*. The data from this work are being used to create databases

for heterocyclic amines and polycyclic aromatic hydrocarbons. If you have an interest in investigating the role of meat cooking practices on these carcinogens in cooked meats, contact Dr. Sinha on 496-6426. (*Sinha R, Knize MG, Salmon CP, Brown ED, Rhodes D, Felton JS, Levander OA, Rothman N. Heterocyclic amine content of pork products cooked by different methods and to varying degrees of doneness. Food and Chemical Toxicology, in press; Sinha R, Rothman N, Salmon CP, Knize MG, Brown ED, Swanson CA, Rhodes D, Rossi S, Felton JS, Levander OA. Heterocyclic amine content in beef cooked by different methods to varying degrees of doneness and gravy made from meat drippings. Food and Chemical Toxicology, in press.)*

Dr. Nancy Potischman was invited to speak at the Cornell University Institute for Comparative and Environmental Toxicology symposium. Her presentation, "The Science that Drives Policy: Pesticides, Diet and Breast Cancer Risk," covered the theoretical basis and review of the epidemiologic evidence linking *in utero*, postnatal and adolescent dietary exposures to risk of adult breast cancer.

In October, Dr. Potischman and Dr. Regina Ziegler participated in a workshop entitled, "The Role of Epidemiology in Determining when Evidence is Sufficient to Support Nutrition Recommendations." The workshop was organized by the International Life Sciences Institute (ILSI), which is an industry-based foundation established to advance understanding of issues related to nutrition, food safety, toxicology and the environment. Dr. Potischman presented a paper with Dr. Douglas Weed of the Division of Cancer Prevention entitled, "Causal Criteria in Nutritional Epidemiology."

In November, Drs. Swanson and Ziegler participated in a Physical Activity and Breast Cancer workshop, co-chaired by Dr. Brinton. The meeting, held in Albuquerque NM, was sponsored by the PHS Office on Women's Health, the American Cancer Society, the National Action Plan on Breast Cancer and the Susan G. Komen Breast Cancer Foundation. Manuscripts summarizing major areas of focus (e.g., epidemiologic issues, exposure assessment, possible biological mechanisms) will be published early in 1998. Dr. Ziegler is interested in following up this workshop with one on research approaches to evaluate the role of energy balance in cancer etiology, and welcomes suggestions and collaborators.

In December, Dr. Ziegler traveled to France to participate in preparing the second handbook in the new International Agency for Research on Cancer (IARC) series on cancer prevention. The topic was individual carotenoids, and Dr. Ziegler chaired the evaluation of human studies, including clinical trials.

Dr. Capri-Mara Fillmore recently participated in a study tour on health problems of workers in Ukraine as a part of the Young Investigators Program sponsored by the National Academy of Sciences. The group toured mining hospitals, company-owned rehabilitation sanatoriums, and coal mines. Ukraine has some of the deepest coal mines in the world, including one 2,500 feet underground, which was a part of the tour. Dr. Fillmore's trip to Ukraine stimulated her interest in the relation of mining exposures and cancer.

Ms. Stephanie Weinstein was selected to participate in the Student Workshop on Epidemiologic Methods, which ran in conjunction with the Annual Meeting of the Society for Epidemiologic Research, held in Edmonton, Alberta, Canada, this past June.

The Branch has added two new staff members: Dr. Arthur Schatzkin and Dr. Ellen Velie. Dr. Schatzkin, who was a member of the intramural Cancer Prevention Studies Branch of DCPC for 13 years, is well known to investigators in DCEG, having collaborated on many projects. He will continue to work on several diet-cancer projects, including:

1) The Polyp Prevention Trial, a randomized controlled trial of the effect of a low-fat, high-fiber, high-fruit and vegetable diet on recurrence of colorectal adenomatous polyps. The first round of that study ends next spring, and a continued follow-up phase is in the works.

2) The NIH-American Association of Retired Persons (AARP) Diet and Health Study, which is a new cohort of some 540,000 men and women (aged 50-69), who responded to a food frequency questionnaire. Some 3,000 breast, 4,000 colorectal, and 5,000 prostate cancers are expected over five years. Work is in progress to develop a biospecimen component. A second questionnaire has been developed to evaluate past diet, physical activity, body size, family history, and medication history. The Branch welcomes ideas for analysis.

3) Dr. Schatzkin is also conducting a study of diet in relation to breast/colorectal cancers as part of the Breast Cancer Detection and Demonstration Project (BCDDP). A new cohort (through 93-95) is now available for dietary analyses, with about 1,000 breast cancers and 300-400 colorectal cancers. Dr. Schatzkin is also working on the Framingham Heart Study, the NHANES follow-up study, and the VA cooperative study on colorectal adenoma risk factors. Dr. Schatzkin is located in EPN 211J, and can be reached at 594-2931.

Dr. Ellen Velie is a new fellow in the Division of Cancer Prevention, who completed her Ph.D. in nutritional epidemiology from the University of California at Berkeley, where she worked with Professor Gladys Block. She will be precepting with Dr. Schatzkin and will participate in the BCDDP follow-up study, examining dietary intake patterns and

breast cancer risk.
.....by Stephanie Weinstein

Occupational Epidemiology Branch

Conference on Women's Health

The Branch is co-sponsoring an international conference on Women's Health in Reykjavik, Iceland, May 14-16, 1998. The conference, entitled "Occupation, Cancer and Reproduction," is a follow-up to a highly successful one sponsored by NCI in 1993. Dr. Shelia Zahm serves on the Conference Organizing Committee and may be contacted for additional information.
.....by Aaron Blair

Breast Cancer Risk and Lifetime Occupational History

Previous studies reported an increased risk of breast cancer among women in professional and managerial occupations. This was recently evaluated in a case-control study that had complete occupational histories and could adjust for reproductive and other risk factors. No association was found for premenopausal women whose major job was a managerial or professional occupation, but an inverse relationship was noted between premenopausal breast cancer risk and having ever held a professional or managerial job (OR=0.53, 95% CI=0.34-0.82). Postmenopausal breast cancer was not related to professional and managerial employment. (*Petralia SA, Vena JE, Freudenheim JL, Marshall JR, Michalek A, Brasure J, Swanson M, Graham S. Breast Cancer risk and lifetime occupational history: Employment in professional and managerial occupations. Occup Environ Med, 55:43-48, 1998)*
.....by Sandra Petralia

Viral Epidemiology Branch

HHV8 -- the Newest Herpesvirus

When new, potentially oncogenic viruses are found, the Viral Epidemiology Branch (VEB) becomes very attentive. Add to this that a virus is associated with Kaposi's sarcoma (KS), one of VEB's major interests, and you have its total involvement. Sought for many years without success, the virus was finally found two years ago by Drs. Yuan Chang and Patrick Moore at Columbia University. Using the new representational difference analysis (RDA) technique in which normal and KS DNA were mixed, the anomalous gene fragments were amplified, and the sequences were compared to GenBank information. In this case, Drs. Chang and Moore found a unique fragment related to Epstein-Barr virus. Further studies extended knowledge of the virus genome and confirmed it to be a new member of the herpesvirus family. The eighth known herpesvirus is called human herpesvirus 8 (HHV8) or Kaposi's sarcoma herpesvirus (KSHV).

This discovery spawned a large number of new studies, mostly molecular in nature, in which new PCR-based assays were developed. The link to KS was rapidly confirmed as virtually solid, with HHV8 detected in almost every KS tumor, although at low copy number. Furthermore, HHV8 also was strongly linked to a rare effusion lymphoma that can affect the pleural, pericardium or peritoneum, and with Castleman's disease, a lymphoproliferative condition. Exciting but questionable links have been made to multiple myeloma, and the virus has been detected in prostate tissue and neural ganglia. So, the search continues.

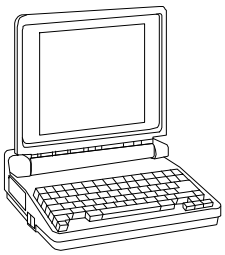
HHV8 must have a natural reservoir in the population. To understand the epidemiology, PCR-based tests are probably inadequate. Only half of the KS cases have detectable HHV8 in peripheral blood mononuclear cells, although all KS patients probably have the virus in their tumors. In response, several laboratories have developed antibody assays, which should provide a more accurate profile of infection history. They are still in development and so far appear to be both moderately insensitive and variably non-specific. However, they do yield data showing that 2 to 20% of the general U.S. adult population has been infected with the virus.

In the past few months, VEB has set up the capability to do PCR. In addition, the Branch is developing a quantitative PCR-based assay, which should further the understanding of the pathobiology of this virus. Furthermore, VEB has established an IFA for detecting antibodies to the virus, which provides results comparable to other tests. Although all tests appear to be somewhat insensitive, they will improve, and VEB is positioned to be a leader in this field.

Thus far, a large number of Kaposi's sarcomas have been screened for different types of lymphomas, prostate cancers, and multiple myelomas for HHV8 antibodies. The expected relationship of the virus to KS was found, but no association was seen with other tumors. VEB does not yet have effusion lymphomas or Castleman's disease specimens to test. The Branch is now applying the antibody assays to several sets of sera banked from its earlier studies, including cohorts of homosexual men and normal populations from areas of Africa and Italy with high rates of KS. These studies should yield exciting findings about the natural history and epidemiology of HHV8.

VEB welcomes collaborations with other groups with an interest in this virus or the associated diseases.
.....by Robert Biggar

INFORMATION TECHNOLOGY



DCEG News Bytes

$UN $ystem $avings Demonstrated

Recently, DCEG purchased a SUN UltraSPARC server to function as an additional platform for supporting DCEG projects. The SUN system is maintained in the Silver Spring offices of IMS, Inc. Use of the SUN was also projected to reduce DCRT batch processing costs. Analysis of the first four months of operation, from August 1997 through November 1997, illustrates that the $110,000 purchase price of the SUN has been recovered in under four months.

During the first four months of operation, the SUN system has been utilized to execute a large number of routine SAS jobs, to process a large data management application, and to analyze the datasets associated with several new smaller studies. A suite of programs was executed at DCRT and on the SUN to define the correct formula for calculating cost savings. Savings were calculated based on actual DCRT batch processing costs and on savings derived from projects that were initiated on the SUN.

From August through November, the monthly DCRT batch processing costs and SAS software licensing fees for IMS have been reduced by a total of $24,600. In addition, the SUN configuration was used to process the 28 million record Veterans Administration (VA) file and several new projects, such as the CER Swedish Occupational Study. The last time that the VA processing was undertaken several years ago, the DCRT costs were over $150,000 for this system alone. Savings on the processing contribute to the recovery of the purchase price of the SUN workstation, since it would have been performed at DCRT had the SUN not been available.

The next quarterly cost savings report, scheduled for March, will reflect the porting of several of the major analysis systems, including the O/E System, to the SUN workstation.

System Implemented to Track Project Costs

Effective January 1998, DCEG implemented project-level cost reporting by individual investigator. This system will compile and report information about the total cost of conducting DCEG studies. Data from the system will be useful in responding to NCI and Congressional inquiries and will help in planning the future research program of the Division. Project-level cost reporting requires input from all resource contractors providing support to DCEG and also will involve the collection of monthly charges for DCRT batch processing, as well as project related costs for travel, equipment purchases, and other miscellaneous expenses.

This reporting system requires that every investigator have a valid set of DCRT initials and that each DCEG study be assigned a unique project code. The draft DCEG Project Tracking Codes are available and will be maintained on WYLBUR at *ucf1www.dceg.project.codes*. Contact Mike Stump in EPN 531 to report new projects, new investigator initials or to get further details about the reporting system.

BSI - II System Development Underway

The final design of the Biological Specimen Inventory System - II (BSI-II) was presented and approved at the December meeting of the DCEG Repository Group. BSI-II is an upgrade of the current system utilized to track and report on biological specimens maintained in repositories that participate in the research program of the Division. The re-engineered portable BSI-II will be implemented using state-of-the-art computer technology based on a graphical user interface and Web features to provide cross-platform access from a wide variety of physical locations in the United States. BSI-II will provide for real-time data collection, quality control, requisition, and reporting. The system will be flexible and applicable to other inventory systems, and be easily installed at other repositories sponsored by the DCEG.

BSI-II is scheduled for implementation during the summer of 1998.

.....by Michael Stump

ADMINISTRATIVE UPDATES

Administrative Resource Center

Professional Service Orders and the Automated Clearing House

In 1998, Professional Service Contractors (PSC) will only receive their payments via Electronic Funds Transfer (EFT). Effective January 1998, PSC contractors are required to be enrolled in the Automated Clearing House through the Administration Data Base (ADB) in order to receive payment. Anyone who request payment for PSC contractors will now need to give their purchasing agent greater lead-time to minimize a delay in payment.

Each PSC contractor must fill out an SF-3881 form, which can be accessed on the internet at *http://www.nih.gov/od/ofm/*. Consultants should be advised that payments are subject to the conditions of the Prompt Payment Act and, as such, should be paid within 30 days of the receiving of services in the ADB.

Please contact Ms. Arnold or Ms. Walton in the ARC with questions regarding this change.

The Research Contracts Branch

RCB Web Sites

The Research Contracts Branch has two internal web sites, which should prove to be useful to DCEG Project Officers. The first site, located at *http://rcb-intranet.nci.nih.gov*, has a "forms" icon that contain numerous procurement forms, such as the Project Plan, Project Officer Technical Questionnaire, Project Objectives (NIH-1688), and NIH-402 requisition. Included on this site are the RCB "Orange Book" of Contracting Policy and Procedures, the NIH Manual Issuances, and the Federal Acquisition Regulations as well as other types of information. Hard copies of these forms can still be obtained from the Contract Specialist.

The other RCB web site is more general in nature and give DCEG staff the opportunity of providing the Chief of RCB with comments, questions, complaints, and even compliments. The web site is located at *http://rcb.nci.nih.gov/*. RCB invites you to visit both sites. You are also encouraged to submit comments and suggestions regarding the web sites to Rick Hartman at *Rich_Hartmann@nih.gov*.

.....by Sharon Miller

DCEG PEOPLE IN THE NEWS

Dr. Aaron Blair, Dr. Louise Brinton, and Dr. Kenneth Buetow were given appointments in the Senior Biomedical Research Service in December 1997.

Dr. Joseph F. Fraumeni, Jr. was promoted to Rear Admiral (Assistant Surgeon General) in the Public Health Service on October 1, 1997.

Dr. Alfred G. Knudson, Jr., Acting Director of the Human Genetics Program, received *The Gairdner Foundation Award* on October 24 "for his development of a two-hit mutational hypothesis for the origin of cancer that related hereditary and nonhereditary forms of retinoblastoma and other tumors; this hypothesis has become a paradigm for mutational theories on the origins of cancer that led directly to the concept of suppressor oncogenes." The Gairdner Foundation award was created "to recognize and reward outstanding contributions to medical science by scientists whose work has contributed significantly to improving the quality of human life."

Two DCEG staff members received *NIH Merit Awards* at the NCI Awards Ceremony in November. **Dr. Kenneth Cantor,** from the Occupational Epidemiology Branch, received the award for his innovative and creative research on the carcinogenic risks posed by contaminants in drinking water. **Dr. Thomas Fears,** from the Biostatistics Branch, received the award for exemplary performance as a statistical collaborator on studies of survivors of childhood cancer, skin cancer, and assay reliability.

Dr. Sandra Petralia, a DCEG Fellow in the Occupational Epidemiology Branch, was a winner of the NIH FARE (Fellows Awards for Research Excellence) competition in 1997. The award recognizes outstanding research and provides funding to attend a scientific meeting. Dr. Petralia's winning research paper is entitled, "Premenopausal breast cancer risk associated with occupational exposure to PAH and benzene."

NEW FACES

Dr. Ahmedin Jemal recently joined the Descriptive Studies Section of the Biostatistics Branch as a Cancer Research Training Award (CRTA) Fellow, and will focus on investigating the geographic variations in cancer mortality, as presented in the forthcoming atlas and identifying potentially relevant correlates using a variety of geographically-based datasets. He is located

in EPN/403 and can be reached at 496-3233.

Ms. Samantha "Sam" Nhan, recently joined DCEG as a secretary in the Office of the Director. In August, she received a B.A. degree in psychology from the University of Maryland. While a college student, Ms. Nhan worked part-time in a support position at the National Institute of Neurological Disorders and Stroke. She can be reached at 594-7161.

Dr. Jackie Prince, a post-doctoral fellow in the Occupational Epidemiology Branch, received a Ph.D. in industrial health from the University of Michigan, and will be contributing to the exposure assessment efforts in several occupational investigations. Dr. Prince is located in EPN/415 and can be reached at 402-9850.

Dr. EllenVelie, a DCP Cancer Prevention Fellow, has begun work in the Nutritional Epidemiology Branch with Dr. Arthur Schatzkin as her preceptor. She received a Ph.D. in Epidemiology, with a focus in nutrition from the University of California, Berkeley. Dr. Velie is located in EPN/443 and can be reached at 435-8431.

Ms. Nancy Weissman, who has a Masters of Science and Social Work, recently joined DCEG as a licensed Clinical Social Worker. She is working with the Genetic Epidemiology Branch on the psychosocial aspects of genetic testing. Located in EPN/531, Ms. Weissman can be reached at 435-4628.

CALENDAR OF EVENTS

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

DATE	MEETING
Feb. 3-4	National Cancer Advisory Board Bldg. 45/E1/E2
Feb. 12	DCEG Seminar, 10:30-12:00, EPN/J
Feb. 19	Senior Advisory Group 2:30-4:30 p.m., EPN/H
Feb. 25	Town Meeting with Dr. Klausner 2-4 p.m., EPN/G
Mar. 2&3	Board of Scientific Counselors- A Bldg. 31/6th flr. conf. ctr.
Mar. 4-6	American Society of Preventive Oncology Annual Meeting Hyatt Regency Hotel, Bethesda
Mar. 5	DCEG Seminar, 10:30-12:00, EPN/J
Mar. 12	Senior Advisory Group 2-4 p.m., EPN/H
April 2	DCEG Seminar, 10:30-12:00, EPN/J
April 6-8	Second National AIDS Malignancy Conference, Bethesda
April 7	DCEG Women Scientists Brown Bag Lunch, Noon, EPN/H
April 9	Senior Advisory Group 2-4 p.m., EPN/H
May 5	DCEG Seminar, 10:30-12:00, EPN/J
May 11-13	National Cancer Advisory Board Bldg. 45/E1/E2
May 14	Senior Advisory Group 2-4 p.m., EPN/H
May 14-16	Women's Health: Occupation, Cancer and Reproduction Reykjavik, Iceland Contact: Dr. Sheila Zahm 496-8157
June 11	Senior Advisory Group 2-4 p.m., EPN/H
Jun. 15	DCEG Women Scientists Brown Bag Lunch, Noon, EPN/H

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Pat Evans - OD/ODOA	**Michael Stump - OD/ODOA**
Mitchell Gail - BB	**Stephanie Weinstein - NEB**