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DIRECTOR'S PAGE

Defining Value-added Science

With increasing budgetary constraints facing NCI and NIH, the Intramural Research Program (IRP) is being challenged to conduct outstanding "value-added" science that can be differentiated from research carried out in the extramural community. It is important, therefore, to define value-added science in the context of the DCEG research program.

As illustrated in the figure on page 2, there are at least three characteristics of the IRP, and DCEG in particular, that enhance our ability to conduct high-impact, high-quality science that is distinctive and value-added in nature.

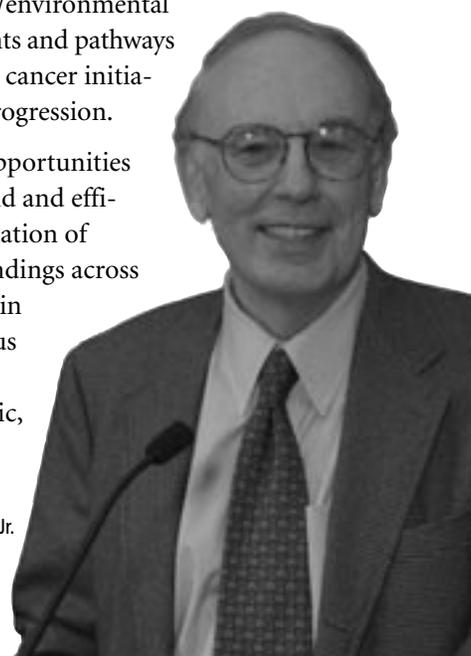
National Agency Mission

- Mandates that the epidemiologic research programs of the Division support and inform the multifaceted initiatives of NIH, including those directed toward the NCI Challenge Goal of eliminating the suffering and death due to cancer.
- Enables the Division to develop and promote large-scale intramural/extramural partnerships in a concerted effort to accelerate progress in molecular epidemiology (e.g., NCI Consortium of Cohorts).
- Provides special opportunities to join forces with other agencies as well as other nations to fully leverage unique resources, to investigate unusual patterns of exposure and cancer occurrence in informative study populations, and to study "natural experiments" whenever and wherever they may occur (e.g., Chernobyl).

- Requires the Division to design and conduct certain studies that address complex, sensitive, and controversial scientific questions that may have important policy or regulatory implications, and to do so in a neutral and authoritative manner (e.g., Congressional and Departmental mandates).
- Enables the pursuit of important research opportunities that otherwise may go unattended (e.g., rare diseases, studies in high-risk populations identified on the NCI cancer mortality maps).

Breadth and Depth of Expertise and Resources Across NCI and NIH

- Enables the development of multidisciplinary infrastructures for cutting-edge collaborative research at the intersection of clinical, basic, and population sciences.
- Fosters the inclusion of genomic and other emerging technologies into epidemiologic study designs with the power to uncover the genetic/environmental determinants and pathways involved in cancer initiation and progression.
- Provides opportunities for the rapid and efficient translation of research findings across disciplines in the IRP, thus expediting the scientific,



Joseph F. Fraumeni, Jr.

DCEG Linkage

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clinical, and public health impact of research initiatives (e.g., HPV studies including vaccine trial).

- Enables collaborative research and resource-sharing with groups in other Divisions and Institutes engaged in population and public health sciences, including the epidemiology of diseases other than cancer.
- Provides the research resources and the senior faculty for highly distinctive postdoctoral and predoctoral fellowship and tenure-track programs, including those of an interdisciplinary nature.

Relatively Stable Funding with Critical Mass of Expertise in DCEG

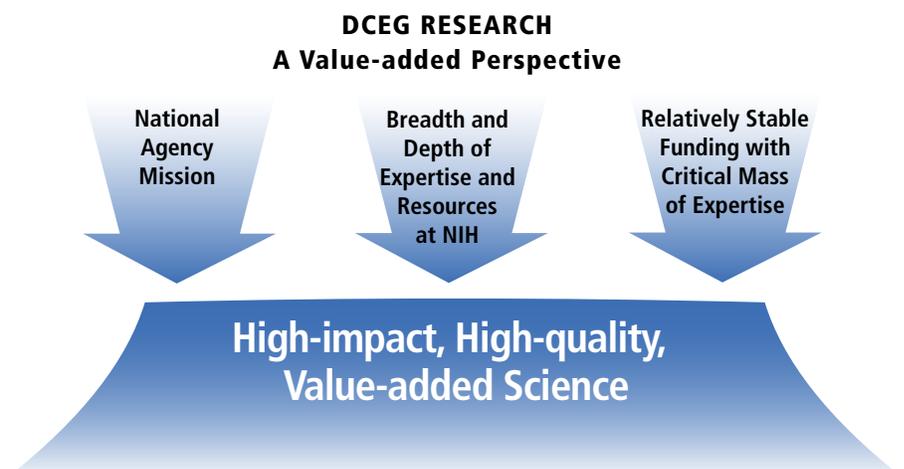
- Enables the conduct of high-risk or long-term projects that are difficult to carry out in the extramural community.
- Provides the capability for rapid and efficient responses to emerging scientific and public health questions.
- Sustains a highly interactive community of investigators with complementary backgrounds and skills.
- Promotes critical methods research and the development of “tools and resources” that are publicly available on the DCEG web site and that catalyze research in the extramural as well as intramural communities.

- Supplies an integrative epidemiologic framework to address NCI strategic research initiatives, extending beyond molecular epidemiology to cancer detection and prevention, integrative biology, health disparities, and other areas of clinical and public health importance.

The Goal: High-impact, High-quality, Value-added Science

The aforementioned characteristics of the IRP at the level of NIH, NCI, and DCEG have enabled the Division to develop and sustain a broadly based research portfolio that ranges from highly distinctive or vanguard research projects to large-scale team-based consortia involving strategic partnerships with the extramural research community. The impact and quality of the research portfolio depend to a considerable extent on vibrant fellowship and tenure-track programs that attract, nourish, and inspire the new generation of epidemiologists and other scientists with an interdisciplinary perspective. When all is said and done, it is the ability to galvanize cancer research on a national and international scale, and to complement rather than duplicate work in the extramural research program, that is the hallmark of the DCEG and NCI value-added scientific enterprise. ■

—Joseph F. Fraumeni, Jr., M.D.



DCEG INTERNET PORTALS

Epidemiologists lead and participate in studies that involve multiple disciplines, centers, and investigators, making it a challenge just to coordinate communication between individuals, let alone conduct research. To ease this burden, **Patricia Hartge, Sc.D.**, and **Geoffrey Tobias** in the Epidemiology and Biostatistics Program are working with contractors at Information Management Services (IMS) to make communication portals the norm for DCEG researchers.

Portals are already up and running for two different projects on non-Hodgkin lymphoma—one is a cooperative case-control study between NCI and SEER, and the other is a consortium of which the NCI-SEER study is a member. The portals contain features such as group distribution lists, a message board, and a calendar with the capacity to embed meeting agendas and minutes. The portals also serve as repositories for many essential documents, such as Institutional Review Board protocols and published papers. Dr. Hartge, principal investigator (PI) on the NCI-SEER study, remarks that “we just have to use this type of technology for intra-study communication. This way, everyone has access to the same information. We can all look at the same data at the same time.”

The portals can be tailored to each study’s specific needs; however, much time has been spent to create a template that will work generally for all studies across the Division. The use of a portal can eliminate the need for e-mailing multiple drafts or datasets to colleagues and streamline maintenance of contact information. All the information is stored in one central location to which the necessary researchers have access and can update as needed.



Patricia Hartge and Geoffrey Tobias

Dr. Hartge is so satisfied with how the portals are working for her that she wants everyone who struggles in similar large studies to benefit as well. At first she casually mentioned the idea to co-workers. Now she invites them to presentations of her portals and discusses with the PIs their needs and how portals can benefit them. Mr. Dave Hacker and other computer experts from IMS are

usually on hand to discuss how each study’s needs can be met. Mr. Tobias, who helps to maintain and update the two current portals, adds, “We’re the template. We’re laying the groundwork to make creation and use of study-specific portals as easy as possible for others. Every study can benefit from a portal.” ■

—Cari Kornblit

FIRST LADY OF UKRAINE VISITS NIH

hor J. Masnyk, Ph.D., and **Alina Brenner, M.D., Ph.D.**, members of the Radiation Epidemiology Branch, represented NCI at a meeting with the First Lady of Ukraine, Mrs. Kateryna Yushchenko, held in April at the office of the DHHS Special Assistant to the Secretary for International Affairs, Dr. William R. Steiger. Opening comments were made by Dr. Steiger and Dr. Sharon Hrynkow, Acting Director, Fogarty International Center, NIH, followed by presentations from NIH scientists. Dr. Masnyk reported on the Ukrainian-American Thyroid Cancer Project, which recently completed its third cycle of thyroid disease screening among a cohort of 13,000 individuals who lived in the Chernobyl area at the time of the nuclear reactor accident in 1986. The subjects were between 0 and 18 years old at the time of the incident, and their radiation doses to the thyroid were measured. Participation in the screening program has been maintained at over 90 percent, and a fourth two-year screening cycle is planned. Dr. Brenner then presented the perspective of a junior Ukrainian scientist working at NIH. In addition to the NCI scientists, Dr. Faye Calhoun (NIAAA) and Dr. Nora Volkov (NIDA) also briefed the First Lady. In closing, Mrs. Yushchenko shared her thoughts and plans for a dynamic program in health research and education, scientific exchange, and modernization of the Ukrainian health care system.



Kateryna Yushchenko

RADIOLOGIC TECHNOLOGISTS COHORT

When **Alice Sigurdson, Ph.D.**, interviewed at NCI and heard about the U.S. Radiologic Technologists (USRT) study, she was immediately drawn to it. Since joining the Radiation Epidemiology Branch (REB) in September of 1999, Dr. Sigurdson has focused her efforts on developing the genetic components of the study.

The USRT is a cohort study of more than 146,000 radiologic technologists from across the country. Begun in 1982, it is a collaborative effort among NCI, the University of Minnesota School of Public Health, and the American Registry of Radiologic Technologists. The largest study of its kind, its primary goal is to determine the risk of cancer from chronic low-to-moderate doses of ionizing radiation. While most previous studies of radiation-exposed workers were done in predominantly male populations, 73 percent of this study's participants are female. **Michele Doody, M.S.**, an REB staff scientist who has worked on the USRT study since 1984, stresses, "This study can provide more definitive



Alice Sigurdson

risk estimates for breast and other cancers in women and men exposed long-term to low radiation doses than has been possible to date."

Dr. Sigurdson's main interests lie in the genes involved in sensing and repairing DNA damage caused by radiation exposure, particularly in relation to breast cancer. Dr. Sigurdson explains, "It really

boils down to finding factors that make people more or less susceptible to damage from radiation. That's what makes me get up in the morning—thinking that I might make a dent in that." Toward making that dent, Dr. Sigurdson has collected blood samples to study the role of certain inherited genes in breast cancer. This nested case-control study within the cohort now has samples from 900 women with breast cancer and 1,100 age-matched controls.

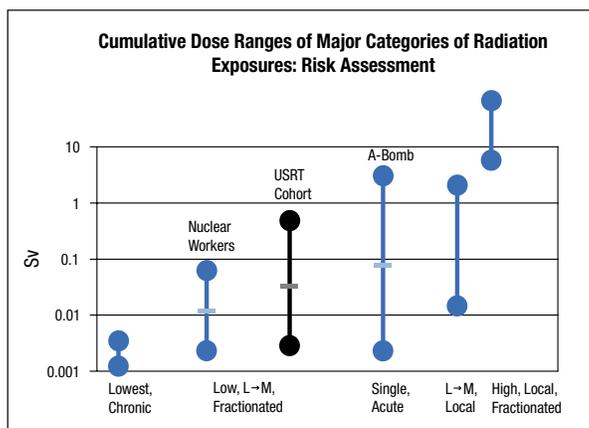
Among the many genes that Dr. Sigurdson plans to evaluate are XRCC1 and DNA-PKcs. XRCC1 is a scaffolding protein in the base excision repair pathway that helps form multiprotein complexes that repair single-stranded DNA breaks typical of those induced by ionizing radiation. DNA-PKcs, the catalytic subunit of a DNA protein kinase, is involved in repairing double-strand DNA breaks and in telomere stability. Researchers studying a strain of mouse that is susceptible to radiation-induced mammary tumors found polymorphisms in the mouse gene equivalent to DNA-PKcs. By studying this gene in women with breast cancer, Dr. Sigurdson hopes to link basic science with population science.

Dr. Sigurdson works closely with Dr. Jeffery Struewing in the Center for Cancer Research and **Michael Hauptmann, Ph.D.**, in the Biostatistics Branch (BB) to examine the genetic determinants of breast cancer. In addition to looking for genetic polymorphisms, Dr. Sigurdson hopes to compare levels and activity of the DNA-PKcs



DCEG's Radiologic Technologists Study Team: (front row) Michael Hauptmann, Steven Simon, Parveen Bhatti, Beth Brown; (back row) Kiyohiko Mabuchi, Mina Ha, Preetha Rajaraman, Jeffery Struewing, Elaine Ron, Michele Doody, Martha Linet, Alice Sigurdson, Isabelle Thierry-Chef, Michal Freedman, Shih-Chen Chang.

proteins among groups of people so as to better understand the role this gene plays in causing a person exposed to radiation to develop cancer. In collaboration with other DCEG researchers, including **Parveen Bhatti, M.S.** (REB), **Michal Freedman, Ph.D.** (REB), **Shih-Chen Chang, Ph.D.**, Nutritional Epidemiology Branch, **Mina Ha, M.D., Ph.D.** (REB), **Preetha Rajaraman, Ph.D.** (REB), **Beth Brown, Ph.D.**, Viral Epidemiology Branch, **Martha Linet, M.D., M.P.H.** (REB), and Ms. Doody, Dr. Sigurdson is looking into genetic polymorphisms in a number of other pathways, including double-strand break repair, nucleotide excision repair, inflammation, metabolism, oxidative damage, and apoptosis.



The mean cumulative radiation dose in the USRT cohort is intermediate between that of the nuclear workers and the A-bomb survivors.

Since it has nationwide distribution, the USRT study also offers an opportunity to study nonmelanoma skin cancer as a result of ultraviolet radiation exposure. Few registries collect skin cancer data. Dr. Sigurdson points out that this cohort “is strongly positioned to describe, characterize, and quantify basal and squamous cell carcinoma risk.” Under the leadership of Dr. Linet, Chief of REB, Dr. Freedman, **Ruth Kleinerman, M.P.H.** (REB), **Kiyohiko Mabuchi, M.D., Dr.P.H.**

(REB), and **Thomas Fears, Ph.D.** (BB), have been pursuing their interests in skin cancer within the USRT study. To accomplish this task, detailed questions on lifetime sun exposure were included in a third survey that has recently been distributed to the whole cohort.

Another series of sun-exposure questions is also being distributed as part of a smaller study to test their reliability and accuracy as an epidemiologic tool. Dr. Linet explains, “These are the same types of questions used by many studies. We want to make sure that from the answers we receive, we can estimate true sun exposure.” The small pilot study will compare responses provided on ques-

tionnaires to UV dosimetry readings taken daily over a weeklong period. This will test how accurately respondents estimate their sun exposure during the week measured, as compared to the dosimetry readings. By sending questionnaires out in six-month intervals and asking the same questions about lifetime exposure twice, researchers will be able to tell how dependable and reproducible the respondents’ answers are.

The USRT cohort offers the scientists involved immense avenues for research. As answers from the third wave of questionnaires come pouring in, and the “pioneers”—workers employed at the earliest time period and thus most highly exposed to radiation—get older, the opportunities grow. Dr. Sigurdson notes that she and other USRT researchers continue to search for collaboration, adding “We can look at things other than

radiation with this cohort. For example, we are evaluating risk factors such as obesity, and we can assess a myriad of outcomes beyond cancer, including osteoporosis, cardiovascular disease, and other aging-related morbidities.” ■

—Cari Kornblit

RECENT FINDINGS FROM THE USRT COHORT

- Breast cancer incidence was significantly elevated in women who had a high index of cumulative radiation exposure.
- Increased incidence of breast cancer, basal cell carcinoma of the skin, malignant melanoma, non-CLL leukemia, and thyroid cancer was related to the year work began and the number of years worked in early calendar years.
- Risks for lung cancer, squamous cell carcinoma of the skin, and other hematopoietic malignancies were not associated with employment factors.
- Polymorphisms in genes whose proteins interact with *BRCA1*, *ZNF350*, and *BRIP1* are unlikely to account for a significant fraction of inherited breast cancer.
- Kin-cohort analyses of breast cancer in first-degree relatives revealed a nonsignificant elevated risk with the proto-oncogene *HER2 (ERBB2)* variant.
- The cell cycle checkpoint gene mutation *CHEK2:1100delC* was more common in breast cancer cases than in controls.

TOWN MEETING RECOGNIZES STAFF ACHIEVEMENTS

In April, DCEG held its eighth annual town meeting with guest speakers Dr. Andrew C. von Eschenbach, NCI Director, and Dr. David J. Hunter, Vincent J. Gregory Professor in Cancer Prevention, Harvard School of Public Health, and NCI Eminent Scholar. Led by **Joseph F. Fraumeni, Jr., M.D.**, Division Director, the meeting also included an awards ceremony recognizing outstanding service and scientific contributions during the past year.



David J. Hunter

Dr. von Eschenbach spoke about the impact of DCEG research on improving health in this country and the world, and he addressed various challenges facing the Institute, including conflict-of-interest regulations, ethics policies, outsourcing, and budget constraints. During an open dialogue, concerns were aired about the future of the Intramural Research Program (IRP) in times of fiscal constraints. Dr. von Eschenbach commended DCEG for its high-impact and high-quality research and encouraged DCEG to continue leading value-added science within the IRP. Examples of DCEG's contributions included the ability to forge large-scale intramural/extramural partnerships to accelerate progress, such as the NCI Consortium of Cohorts and various case-control and family-based consortia.

The NCI Challenge Goal to eliminate the suffering and death due to cancer



Diane Solomon with Andrew von Eschenbach (left) and Joseph F. Fraumeni, Jr. (right).

can be furthered through epidemiologic insights into carcinogenesis that may lead to new preventive strategies including early cancer detection. Dr. von Eschenbach noted that "there is not a more motivated, dedicated group of researchers than the one that exists at NCI. Our workforce exhibits the overarching goal to make a difference that affects society through a true commitment to public service."

Dr. Hunter discussed the state of epidemiology in 2005, reviewing risk factors for various forms of cancer and noting DCEG's contributions to the discovery of etiologic agents, development of risk prediction models and interventions, and delivery of a preventive vaccine and other interventions. In the future, progress in epidemiology will continue to come from well-characterized population-based studies, integration of technological advances, evaluation of inherited susceptibility to environmental exposures, and leverage of the human genome project to understand the causes of cancer. Dr. Hunter discussed the progress and problems in studying gene-environment interactions through the candidate gene approach, and he described a new strategic initiative, the Cancer Genetic Markers of Susceptibility (C-GEMS) project, that will use the cutting-edge technology of whole-genome single-nucleotide polymorphism scans to help identify inherited susceptibility

genes for breast and prostate cancer. C-GEMS is an NCI enterprise activity coordinated by DCEG and the NCI Core Genotyping Facility (CGF), in collaboration with the Cancer Genome Anatomy Project. The overall project goal is to accelerate the discovery of susceptibility or modifier genes in these cancers through a collaborative network, including component studies of the NCI Consortium of Cohorts, with rapid web-based dissemination of results to the entire research community. The project will be coordinated by **Stephen Chanock, M.D.**, Director of CGF, and **Robert Hoover, M.D., Sc.D.**, Director of the Epidemiology and Biostatistics Program (EBP), along with Dr. Hunter.



Sharon Miller with Andrew von Eschenbach (left) and Joseph F. Fraumeni, Jr. (right).

Shelia Zahm, Sc.D., DCEG Deputy Director, served as emcee of the awards ceremony, which began with recognizing the Division's contributions to the 2004 Combined Federal Campaign (CFC). Under the leadership of DCEG coordinator **Elyse Wiszneauckas**, Office of Division Operations and Analysis (ODOA), the Division received its seventh consecutive CFC Presidential Award for meeting 139 percent of its dollar goal, contributing approximately \$35,000, and 111 percent of its participation goal. Branch key workers were **Holly Brown**, Biostatistics Branch, **Patricia Chandler** (ODOA), **Jennifer Connor**, Hormonal and Reproductive Epidemiology Branch



Ann Hsing

(HREB), **Mustafa Dosemeci, Ph.D.**, Occupational and Environmental Epidemiology Branch (OEEB), **Sadie Holmes-Lillie**, Genetic Epidemiology Branch, **Sadie Hutson, Ph.D., R.N., C.R.N.P.**, Clinical Genetics Branch, **Ursula Leitzmann, M.A.**, Radiation Epidemiology Branch, **Tawanda Roy**, Nutritional Epidemiology Branch (NEB), **Julie Russell-Grey**, Viral Epidemiology Branch, and **Michelle Wolfe**, DCEG Administrative Resource Center.

The award for the Outstanding Research Paper by a Fellow, which recognizes a publication during the past calendar year that demonstrated impact, innovation, and clarity of thought and language, was presented to **Jennifer Rusiecki, Ph.D.** (OEEB), for her paper on “Cancer incidence among pesticide applicators exposed to atrazine in the Agricultural Health Study,” which was published in the *Journal of the National Cancer Institute*. **Qing Lan, M.D., Ph.D.** (OEEB), received the award for the Outstanding Research Paper by a Staff Scientist, entitled “Hematotoxicity in workers exposed to low levels of benzene,” which was published in *Science*.

Five fellows received DCEG Fellowship Achievement Awards for outstanding accomplishments: **Amanda Cross, Ph.D.** (NEB), **Marc Gunter, Ph.D.** (NEB), **Lifang Hou, M.D., Ph.D.** (OEEB), **Mark Purdue, Ph.D.** (OEEB), and **Margaret Wright, Ph.D.** (NEB). The winners will receive a two-step annual increase in their NCI fellowship stipend.

This year, two individuals from outside of DCEG received Special Recognition Awards. The first recipient was Dr. Diane Solomon, Division of Cancer Prevention, for her sustained contributions over the past decade to collaborative research projects on the pathogenesis of cervical cancer and on efforts to translate this knowledge to optimal screening and prevention strategies. The work has led to profound revisions in U.S. gynecologic practice and a much better understanding of the relationship between HPV infection and precancer. Her collaborators in HREB noted her rare blend of intelligence, kindness, selflessness, and strength.

The second Special Recognition Award was given to Sharon Miller, NCI Research Contracts Branch, for her exceptional management of DCEG contracts. Ms. Miller has remarkable skills for identifying innovative, cost-effective approaches that allow DCEG scientists to proceed with investigations, many of which involve international field sites



Patricia Hartge with Andrew von Eschenbach (left) and Joseph F. Fraumeni, Jr. (right).

and complex arrangements. One of the Branch Chiefs stated, “Of the many contracting officers with whom I worked over the years, Sharon Miller stands out as the exception in understanding our needs, being willing to work closely with us to overcome difficult arrangements, and minimizing the burden to us so that we can concentrate on our scientific efforts.” Another Branch Chief noted, “I never leave her office or end an e-mail communication without receiving sound advice or a useful answer from Sharon.”



Louise Brinton with Andrew von Eschenbach (left) and Joseph F. Fraumeni, Jr. (right).

The Outstanding Mentor Award honors scientists who demonstrate exceptional skill in and commitment to training and mentoring. There were two winners this year based on the votes from fellows across the Division. **Ann Hsing, Ph.D.** (HREB), was recognized for being “an excellent mentor who motivates fellows to succeed by providing direction, encouragement, and advice. Despite her busy schedule, she meets with fellows on a weekly basis, teaches them to plan ahead to achieve career and personal goals, and shares her experience on managing multiple projects in challenging settings.” **Patricia Hartge, Sc.D.**, Deputy Director of EBP, was recognized for her “fervent support of training and tireless efforts to provide young investigators with a wide range of opportunities in all aspects of research. Her success at mentoring is also due to her personal qualities of carefully listening, respecting others and their interests, having an ‘open door’ policy, and selflessly giving her time and full attention to young investigators.”

Finally, the DCEG Exemplary Service Award went to **Louise Brinton, Ph.D.** (HREB). She was honored for her outstanding research on the epidemiology of female cancers and her sustained service to the Division, Institute, and NIH through skillful management of a large and complex Branch, leadership of several workshops and committees, and devotion to mentoring and training. ■

—Sandy Rothschild

DCEG VISITING SCHOLAR NANCY MUELLER

In February, Dr. Nancy Mueller, Professor of Epidemiology at the Harvard School of Public Health and Associate Director for Population Sciences at the Dana-Farber Cancer Institute, spent two days at DCEG as a Visiting Scholar. Dr. Mueller has had a career of distinguished research investigating the role of viruses in the etiology of cancer. Her work on risk factors for Hodgkin lymphoma laid the foundation for understanding the origins of this tumor. She has also published extensively on a wide range of oncogenic viruses, most notably human T-lymphotropic virus type I (HTLV-I), as well as Epstein-Barr virus (EBV) and hepatitis B and C. During her visit, Dr. Mueller was warmly greeted by colleagues, former students, and friends who have worked with and known her for many years.

Dr. Mueller presented a seminar entitled “Infection and Cancer: What Do We Know and Where Do We Go?” Her presentation focused on the impact of infectious agents on cancer etiology. In developed countries, about 7 percent of cancers are attributed to infections, but

in the developing world, infections cause about 15 percent of cancers. Encapsulating the characteristics of oncogenic viruses, she stressed the importance of chronic persistence of infection as being key to development of malignancy. Viruses capable of persistent infection have evolved mechanisms to drive their host cells to promote the virus, such as by inducing proliferation and blocking cell death. These properties can lead, on occasion, to permanent genetic changes that predispose to cancer. Dr. Mueller stressed the need to study the early events of viral infection and noted the high risk of cancer among persons infected early in life.

Special emphasis was given to the lessons learned from HTLV-I, which causes adult T-cell leukemia/lymphoma (ATL) but, like most oncogenic viruses, does so rarely. Nonmalignant complications, particularly HTLV-associated myelopathy/tropical spastic paraparesis (HAM/TSP), occur at least as often. Typical of viral-associated malignancies, HTLV-I causes ATL decades after infection and is usually acquired during infancy.



Nancy Mueller

Dr. Mueller emphasized the role of the HTLV-I tax gene, which contributes to immortalization and transformation of the infected T lymphocyte. She particularly noted the striking differences in the natural history of HTLV-I infection in two endemic populations—southern Japan, where she led a prospective cohort study in Miyazaki, and the West Indies, where the DCEG Viral Epidemiology Branch (VEB) has conducted complementary research projects. Among HTLV-I–infected carriers in Japan, ATL incidence is much higher than HAM/TSP incidence, while the opposite is true in Jamaica. Furthermore, in Jamaica, the median age at diagnosis of ATL is about 15 years younger than in Japan. Dr. Mueller concluded by emphasizing the importance of understanding the determinants of viral control and other events that occur soon after infection, as these are likely to determine the eventual risk of cancer and other late complications.

On a broader note, Dr. Mueller advocated increasing efforts by DCEG and NCI to build consortia of case-control and cohort studies as the best way to speed advances in cancer epidemiology. Intramural/extramural team science allows creative and innovative science



David J. Hunter

NCI EMINENT SCHOLAR DAVID HUNTER

Dr. David J. Hunter has been appointed as a National Cancer Institute (NCI) Eminent Scholar in the Intramural Research Program (IRP). The scholar program, part of the initiative to re-engineer

and strengthen the IRP, was established to enhance collaboration between extramural and intramural scientists at NCI. Scholars have the opportunity to work in the IRP at NCI and collaborate on key research initiatives, as well as play a direct role in IRP research programs.

Dr. Hunter is the Vincent L. Gregory Professor of Cancer Prevention at the Harvard School of Public Health. He will be located at the NCI Core Genotyping Facility helping NCI scientists develop strategies that apply new molecular technologies (e.g., whole genome scans) to large-scale population studies that seek to uncover susceptibility genes in cancer induction and progression.

to move quickly; provides an intellectually rich environment; can be conducted with relatively little administrative infrastructure; develops buy-in, respect, and trust; and most importantly, opens opportunities for young investigators of the future.

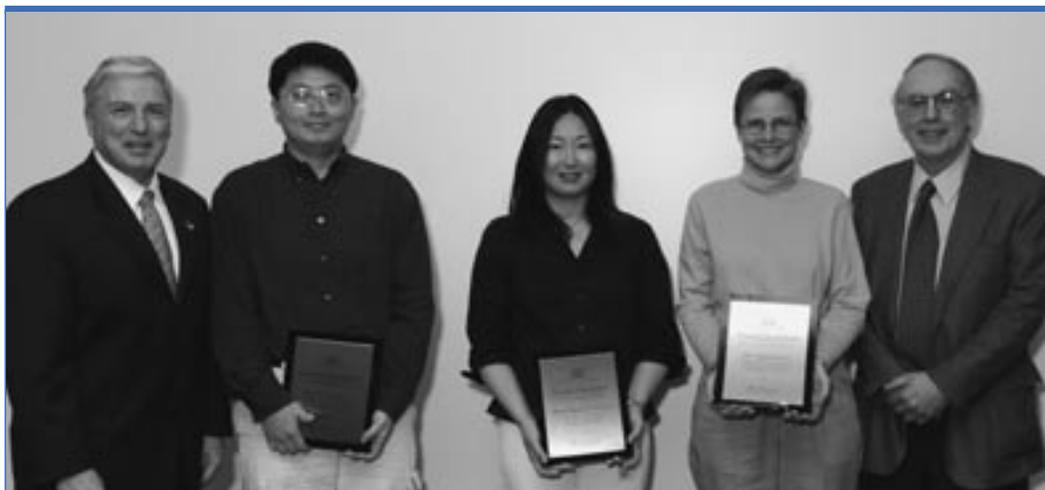
Following the talk, **Joseph F. Fraumeni, Jr., M.D.**, DCEG Director, presented Dr. Mueller with a plaque recognizing her distinguished accomplishments in science as well as her noteworthy contributions to the National Cancer Institute (NCI) as a member of the NCI Board of Scientific Counselors and Board of Scientific Advisors; to the field of epidemiology in which she has worked tirelessly to promote higher standards; and to her students and colleagues, for whom she has been a mentor, role model, teacher, and friend.

During the two-day visit, Dr. Mueller attended meetings with various groups to provide advice on current DCEG research efforts, including discussions on EBV-related studies, led by **Charles Rabkin, M.D.**, VEB; on Hodgkin lymphoma research, moderated by **Lynn Goldin, Ph.D.**, Genetic Epidemiology Branch; and on non-Hodgkin lymphoma research,

facilitated by **Patricia Hartge, Sc.D.**, Epidemiology and Biostatistics Program. In addition, separate meetings were held with fellows, with women scientists (organized by Women Scientist Advisors Dr. Goldin and **Debra Silverman, Sc.D.**,

Occupational and Environmental Epidemiology Branch), and with VEB staff members, hosted by Branch Chief **James Goedert, M.D.** ■

—James J. Goedert, M.D.



Intramural Research Award Recipients: Shih-Chen Chang, Michie Hisada, and Alice Sigurdson with Andrew von Eschenbach (left) and Joseph F. Fraumeni, Jr. (right).

DCEG INTRAMURAL RESEARCH AWARDS

DCEG funds several Intramural Research Awards (IRAs) each year. These competitive awards support innovative and interdisciplinary collaborative research projects (up to \$75,000 per fiscal year, renewable for up to three years) led by tenure-track investigators or postdoctoral fellows. Recipients of IRAs are recognized for their creative ideas in advancing the goals of the NCI. The program was expanded this year to two award competitions (fall and spring), at each of which up to three proposals are funded.

The winners of the fall 2004 competition are **Shih-Chen Chang, Ph.D.**, Nutritional Epidemiology Branch, for his proposal on "Breast cancer risk and circulating vitamin D metabolites and polymorphisms in the vitamin D receptor and hydroxylating enzymes"; **Michie Hisada, M.D., Sc.D.**, Viral Epidemiology Branch, for her project on "Host factors, population admixture, and risk of T-cell non-Hodgkin lymphoma in the Afro-Caribbean"; and **Alice Sigurdson, Ph.D.**, Radiation Epidemiology Branch, for her proposal entitled "Can functional assays prospectively predict lung cancer risk?"

Each application is reviewed by a member of the NCI Board of Scientific Counselors or another scientist outside NIH with appropriate expertise, as well as senior DCEG scientists. Proposals are judged on their potential for significant scientific or public health impact, innovative aspects of the approach or methodology, interdisciplinary and collaborative nature of the project, potential to achieve the objectives within the proposed time frame and resources, and programmatic relevance to the Division and Institute. The award can be combined with funds from other sources to support a larger project.

—Sandy Rothschild



Nancy Mueller with Joseph F. Fraumeni, Jr.

ERIC ENGELS LEADS A TEAM IN THE STUDY OF VIRUS-RELATED CANCERS

Many physicians are committed to combining research and clinical practice ... at least hypothetically. Often, the real-life demands of one or the other make it impossible to forge a dual career. **Eric Engels, M.D., M.P.H.**, is doing it, however. Not only is he a tenure-track investigator in the Viral Epidemiology Branch, but he also sees patients at Johns Hopkins University Hospital.

At NCI, Dr. Engels' research has several aspects. He studies HIV-associated cancers as well as cancers in other immunosuppressed populations, such as transplant recipients. In addition to studies of non-Hodgkin lymphoma (NHL), Dr. Engels has conducted landmark work on simian virus 40 (SV40). His series of epidemiologic studies showed that this virus, a

contaminant of the polio vaccine in the 1950s and 1960s, is not associated with an increased risk of cancer.

Most recently, Dr. Engels has been investigating an apparent excess of lung cancer in people with HIV/AIDS. Better treatment regimens have improved the outlook for patients with AIDS but have also raised other issues, he says. "I'm interested in not just the usual cancers related to HIV, but also cancers that originally were not thought to be linked, such as lung cancer. These cancers now will be an increasing public health burden as people with HIV live longer."

Long interested in mathematics and science, Dr. Engels majored in mathematics at the University of Virginia, graduating

in 1987. "I like solving problems and analyzing data, thinking about models for how things are related," he says. "But it wasn't until college that I wanted to be a physician, combining an interest in medical science with being more involved in the real world, solving problems that affect people's lives."

That combination is still evident in his mix of research and clinical practice. He became increasingly interested in research during his clinical training at Harvard Medical School, from which he graduated in 1991. "Early on, before we had good therapies, I took care of people with AIDS," he explains. "I was struck by the nature of this epidemic and the research and public health implications."

At the start of his research career, he saw an opportunity to work at NCI. Thinking the time would be "a nice interlude," he came to Bethesda in 1998 and never left.

Dr. Engels and colleagues have published nearly a dozen studies examining the possible association between SV40 and tumors suggested by some laboratory studies. In an epidemiologic study of U.S. veterans, no association was found between exposure to SV40-contaminated vaccine and an increased risk of brain tumors, NHL, or mesothelioma. Another recent study found no correlation between SV40 seropositivity and the risk of NHL.

His work on cancers among the immunosuppressed has included studies of Kaposi sarcoma and its causative virus, called human herpesvirus-8 (HHV8) or Kaposi sarcoma-associated herpesvirus (KSHV). "We've done studies in the United States among people with HIV and studies in Africa looking at the epidemiology of the virus, which is very common in sub-Saharan Africa," he notes.



Eric Engels

"I would like to understand the changing patterns in cancer over the next 10 years or so among HIV-infected persons, and the effects of anti-HIV drugs. What is the risk of cancer among people taking these drugs and what cancers are they getting?"

“Now we’re doing a study of Kaposi’s sarcoma in transplant recipients, another population at high risk,” Dr. Engels says. “We have a productive and collaborative group in our branch, looking at every stage along the pathway, from viral infection to cancer.”

Dr. Engels’ clinical practice at Johns Hopkins, he says, keeps him grounded in the realities of living with HIV. “It has allowed me to understand how the therapies affect people’s infection status, how difficult it is to take those medications, why people fail on certain medications... Seeing patients keeps me more connected with the actual day-to-day realities of HIV infection, makes it more real.”

Seeing patients has also shaped his research questions. “One example is lung cancer research,” he says. “I’m acutely aware that my patients with HIV infection tend to smoke, and many have developed smoking-related cancers. So we are collaborating with the Hopkins group to understand etiologic mechanisms in lung cancers, that appear excessive in AIDS patients and do not appear to be entirely attributable to smoking. It’s a provocative finding that is pushing me to look at lung cancer more intensively.”

Long-term, he answers, “I would like to understand the changing patterns in cancer over the next 10 years or so among HIV-infected persons, and the effects of

anti-HIV drugs. What is the risk of cancer among people taking these drugs and what cancers are they getting?” Also on the horizon is more research with other immunosuppressed populations, such as transplant recipients. “I’d like to understand how immunity and inflammation play a role in the development of lung as well as other cancers. One avenue I see is exploring pathways of inflammation and immunity in the general population, as well as in high-risk groups for various cancers through molecular epidemiology.” ■

—Nancy Volkers

PREDOCTORAL FELLOWS JOURNAL CLUB

The Predoctoral Journal Club was initiated in late 2004 by **Gabriella Andreotti, M.P.H.**, of the Hormonal and Reproductive Epidemiology Branch (HREB), and **Sarah Daugherty, M.P.H.**, of the Occupational and Environmental Epidemiology Branch (OEEB). Both are CRTA predoctoral fellows and doctoral candidates at George Washington University and Johns Hopkins Bloomberg School of Public Health, respectively. Due to the nature of the full-time fellowships, many predoctoral fellows are unable to attend the journal clubs sponsored by their university. Therefore, Ms. Andreotti and Ms. Daugherty organized a group that would draw from the rich resources available to predoctoral fellows in DCEG. The goal of the journal club is to encourage cross-disciplinary discussions on a variety of topics of interest to the fellows.

So far, the journal club has met monthly. Each meeting is hosted by a rotating moderator who selects an article and invites a DCEG senior scientist with expertise in the topic of interest. Subjects have included: false-positive report probability; test reliability and measurement error, using a human papillomavirus study as an example; obesity and hormones; second cancers after radiotherapy; regression tree analysis; and poisson and cox regression. As of April, discussions have been led by **Montserrat Garcia-Closas, M.D., Dr.P.H.** (HREB), **Sholom Wacholder, Ph.D.**, Biostatistics Branch (BB), **Mark Schiffman, M.D., M.P.H.** (HREB), Dr. Rudolf Kaaks, International Agency for Research on Cancer, **Alice Sigurdson, Ph.D.**, Radiation Epidemiology Branch, **Nilanjan Chatterjee, Ph.D.** (BB), and **Jay Lubin, Ph.D.** (BB). The club is grateful to the senior scientists who have taken the time to meet with the group and hopes to include many others as guest speakers in the future.



DCEG’s Predoctoral Fellows: (front) Michelle Khan and Mark Donahue; (back) Adrienne Katner, Gabriella Andreotti, and Sarah Daugherty. (Not shown: Sonja Berndt, Parveen Bhatti, Joseph Carreon, Benjamin Hulley, Hormuzd Katki, Janet Lee, Lori Sakoda, Sara Schonfeld, Laveta Stewart, Fang Fang Zhang, and Honghong Zhu)

—Gabriella Andreotti, M.P.H., and Sarah Daugherty, M.P.H.

NEW DIGITAL TOOLS FOR VISUAL DATA ANALYSIS

Most studies in DCEG include the collection of text data (e.g., questionnaires, test results) and visual data such as cytology, histology, and pictures of lesions or organs (e.g., nevi, cervigrams—pictures of the uterine cervix). There is a variety of software available for processing text data; however, analysis of visual data is more problematic. For example, to obtain consistent information about a biopsy, it is necessary to send the glass slide to a pathologist, wait for that reading, and then send the same slide to other experts around the United States or overseas. This process is time-consuming, and the glass slide can break or deteriorate during shipping. Similar challenges are faced when evaluating cervigrams, because diagnoses are obtained from one expert at a time and involve shipping hard copies of the images from one expert to another. Also, for both microscopic slides and pictures, it is difficult to quantify specific anatomical details.

New digital tools have been developed in some DCEG projects to collect specific,

detailed information from visual data and share images via the Internet.

Virtual Microscope

A virtual microscope is a tool that scans an entire glass slide of a biopsy and creates a digital file of the tissue section image. These digitized biopsies can be accessed by multiple experts using Web-based tools on the Internet (Figure 1). Reviewers obtain a high-fidelity, highly magnified view of the tissue, which permits them to evaluate the tissue and answer specific questions about the diagnosis as well as architectural and morphological characteristics of the cells. The virtual microscope's digital images do not break; are easy to duplicate and distribute; can be viewed in their entirety at multiple magnifications on a computer screen; allow evaluation through the Internet; eliminate the need for experts to travel for meetings to review images; and provide a permanent image of tissue stains, some of which otherwise fade over time.

The virtual microscope is currently being used for studies of testicular cancer led by **Mark H. Greene, M.D.**, Chief of the Clinical Genetics Branch, and **Mary Lou McMaster, M.D.**, a staff clinician of the Genetic Epidemiology Branch, as well as studies of cervical cancer led by **Jose Jeronimo, M.D.**, a staff scientist of the Hormonal and Reproductive Epidemiology Branch.

Boundary Marking Tool

The boundary marking tool (BMT) is a Web-accessed tool created by Dr. Jeronimo and the National Library of Medicine that allows the systematic collection of data from uterine cervix images by colposcopy experts. The expert is able to mark boundaries around anatomical regions of special etiologic or diagnostic interest, such as the cervical os and squamous-columnar junction. Abnormalities such as acetowhite (dysplastic) epithelium or invasive cancer (Figure 2) can be noted, if they are present. The information collected with the BMT is saved as digital records in a

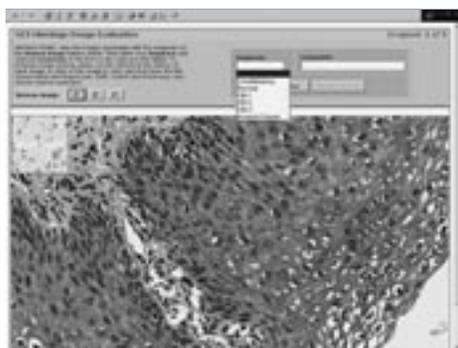


Figure 1. Virtual Microscope: Magnified view of the biopsy and pull-down menu to answer questions and provide a diagnosis.

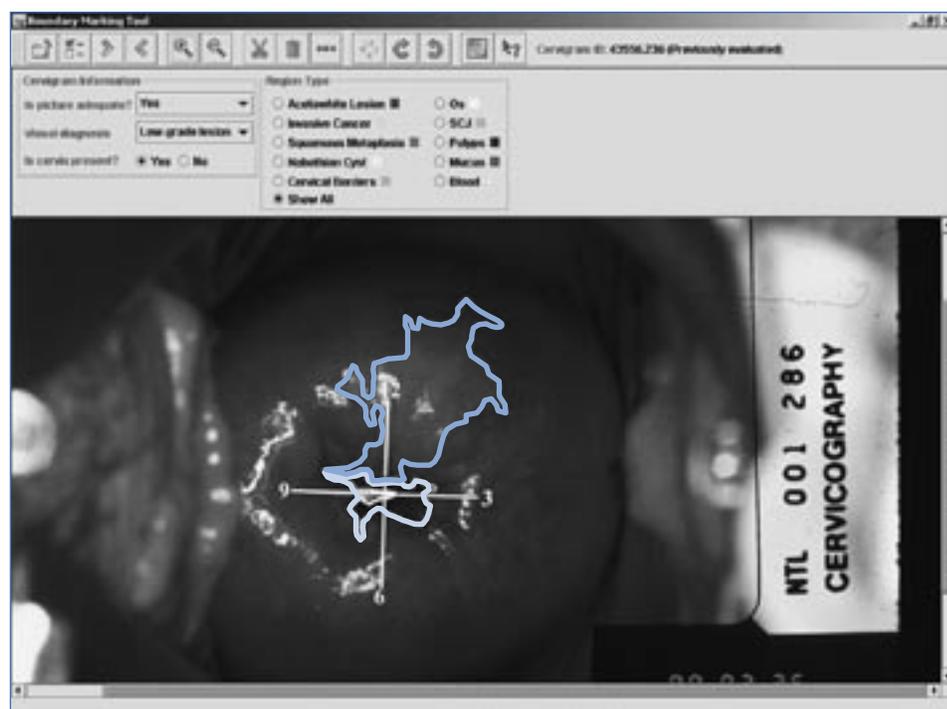


Figure 2. Boundary Marking Tool (BMT): All the information collected is saved in the database. The region outlined in darker blue identifies a dysplastic lesion, while that outlined in lighter blue draws attention to the uterine os. The perpendicular white lines indicate the spatial position of the uterine cervix.

central database. Later, that information can be translated into pixels for use in quantitative epidemiologic studies.

The BMT is being used in DCEG research studies of human papillomavirus (HPV) infection and cervical cancer, in which serial cervigrams are used to explore and understand the changes that occur on the uterine cervix as a consequence of infection with HPV. These changes can be monitored until either the cancer develops or the virus is cleared. Current research also includes exploring the differences in visual manifestations of various types of HPV. Studies on visual characteristics of normal cervixes will provide information about physiological changes in healthy women. The BMT can also be applied to images of other tissues.

Multimedia Database Tool

The multimedia database tool (MDT) is a Web-based system that provides access to images and text data collected during research projects. It can be used as an exploratory tool for retrieving visual and text data according to specific characteristics such as age, parity, and test results. The researcher makes a query, the MDT identifies patients matching those parameters, and then the MDT retrieves and displays the image and text data. The MDT can support a variety of image types, such as digital pictures of malignant lesions, digitized cervigrams, cytology, and histology. The design of the MDT gives it the flexibility to accommodate new datasets, and the study-specific customization can be handled by the database administrator, rather

than the programmer. Additionally, because of its architecture, the MDT system can support a broad class of text/image databases, so it greatly expands the opportunities for collaborative studies.

These tools, developed collaboratively by DCEG staff, allow researchers to incorporate the quantitative and systematic analysis of visual data into epidemiological studies and provide opportunities for collaborative studies with scientists around the world, with subsequent benefits for the nation's health. ■

—Jose Jeronimo, M.D.,
Mary Lou McMaster, M.D.,
and Mark H. Greene, M.D.

NEW BROCHURE ON RADIATION RISKS PUBLISHED

The Radiation Epidemiology Branch (REB) has published *Interventional Fluoroscopy: Reducing Radiation Risks for Patients and Staff*, a brochure for physicians and radiology technicians. Interventional fluoroscopy is a procedure that uses ionizing radiation to guide small instruments such as catheters through vessels or other pathways in the body. Increases in the use and complexity of these procedures, and the resulting exposure of patients and health care personnel to greater amounts of radiation, have raised public health concerns. In conjunction with the Society of Interventional Radiology (SIR), REB investigators **Martha Linet, M.D., M.P.H.**, Branch Chief, **Isabelle Thierry-Chef, Ph.D.**, and **Ruth Kleinerman, M.P.H.**, developed this brochure, which was distributed at the annual meeting of the SIR in New Orleans in April. Others consulted in the production of this brochure include: Dr. David Brenner (Columbia University), Dr. Thomas Shope (Food and Drug Administration), Dr. Donald Miller (SIR), Dr. Fred Mettler (University of New Mexico

Medical School), Dr. Gary Becker (National Cancer Institute), Dr. Victoria Marx (University of Southern California), Dr. Lou Wagner (University of Texas Health Science Center at Houston), and Dr. Steve Balter (Lenox Hill Hospital, New York).

This brochure provides information on the benefits and risks of interventional fluoroscopy. Interventional fluoroscopy represents a huge advantage over invasive surgical procedures, because it requires only a very small incision, substantially reduces the risk of infection, and allows for shorter recovery time compared to surgical procedures. The brochure points out that the intervention is not without risks. There have been reported cases of severe skin burns in patients who have received a high radiation dose. Health care providers are at risk of injuries to the lens of the eye and skin due to chronic exposure to radiation. Long-term effects include the risk of cancer for both patients and health care providers.

A second subject addressed by the brochure is radiation dose and the need for training. Many specialists who perform these procedures have little education in radiation science or protection measures. An important goal of *Interventional Fluoroscopy* is to create awareness of optimal doses of radiation (the smallest amount required to produce adequate image quality and imaging guidance) to patients, which will in turn minimize the radiation exposures of the health care worker. Of critical importance is adequate training of health care providers to use equipment that provides acceptable image quality along with the maximum possible dose reduction.

Copies of the brochure can be obtained from REB or the Branch's Web site: <http://dceg.cancer.gov/radia.html>.

—Abigail Ukwuani, M.P.A.

SCIENTIFIC HIGHLIGHTS

BREAST CANCER

Global Incidence and Mortality Trends

Worldwide, breast cancer is the most common cancer and is the leading cause of cancer death among women. To describe global trends, the authors compared age-adjusted incidence and mortality rates over three decades and across several continents. Both breast cancer incidence and mortality rates varied four-fold between countries with the highest and lowest rates; recent incidence ranged from 27/100,000 in Asian countries to 97/100,000 among U.S. white women. North American and northern European countries had the highest incidence rates; intermediate levels were reported in Western Europe, Oceania, Scandinavia, and Israel; and Eastern Europe, South and Latin America, and Asia had the lowest levels. Breast cancer incidence rose 30%–40% from the 1970's to the 1990's in most countries, with the most marked increases among women aged 50 years and older. Mortality from breast cancer paralleled incidence: it was highest in the countries with the highest incidence (between 17/100,000 and 27/100,000), lowest in Latin America and Asia (7–14/100,000), and rose most rapidly in countries with the lowest rates. Breast cancer incidence and mortality rates remain highest in developed countries compared with developing countries. (Althuis MD, Dozier JM, Anderson WF, Devesa SS, Brinton LA. Global trends in breast cancer incidence and mortality 1973–1997. *Int J Epidemiol* 2005;34:405–412)

CERVICAL CANCER

Mortality and Incidence Trends

In the United States, increased detection of squamous carcinoma *in situ* (CIS) by screening has led to reduced rates for invasive squamous carcinoma and lower mortality. Adenocarcinoma *in situ* (AIS) rates also have increased, but invasive

cervical adenocarcinoma rates have not declined similarly. To make inferences about the effectiveness of screening, the authors used data from the Surveillance, Epidemiology, and End Results (SEER) Program to tabulate incidence for invasive carcinomas (1976–2000) and for CIS and AIS (1976–1995) by age and race. Cumulative relative survival rates were tabulated for 1976–1995 and mortality rates were estimated for 1986–2000. Among all groups, CIS rates approximately doubled, whereas rates for invasive squamous carcinoma declined. Although AIS rates have increased dramatically among whites (all ages) and younger blacks, adenocarcinoma incidence and mortality rates have not changed greatly. Survival for patients did not change greatly within these age-race groups. Increases in CIS seemed disproportionately large compared with improvements in mortality rates for invasive squamous carcinoma. Despite increased reporting of AIS, declines in mortality for cervical adenocarcinoma have not been demonstrated. (Sherman ME, Wang SS, Carreon J, Devesa SS. Mortality trends for cervical squamous and adenocarcinoma in the United States. *Cancer* 2005;103:1258–1264)

COLORECTAL ADENOMAS

Effect of *CYP1A1* and *NQO1* Variants

Cigarette use is a risk factor for colorectal adenoma, a precursor of cancer. Polymorphic variants in *NQO1* and *CYP1A1* influence the activation of carcinogenic substances in tobacco smoke, possibly impacting tobacco-associated risks for colorectal tumors. Subjects were 725 non-Hispanic Caucasian cases with advanced colorectal adenoma of the distal colon (descending colon, sigmoid, and rectum) and 729 gender- and ethnicity-matched controls, randomly selected from participants in the Prostate, Lung, Colorectal, and Ovarian

Cancer (PLCO) Screening Trial. The polymorphic variants *CYP1A1 Val₄₆₂* and *NQO1 Ser₁₈₇* individually were weakly associated with risk of adenoma, but subjects carrying both alleles showed increased risks (OR = 2.2; CI = 1.1–4.5), particularly among recent (OR = 17.4; CI = 3.8–79.8; *p* for interaction = 0.02) and heavy cigarette smokers (> 20 cigarettes/day) (OR = 21.1; CI = 3.9–114.4; *p* for interaction = 0.03) compared with nonsmokers who did not carry either of these variants. The combined gene variants were most strongly associated with the presence of multiple adenomas (*p* = 0.002). (Hou L, Chatterjee N, Huang WY, Baccarelli A, Yadavalli S, Yeager M, Bresalier RS, Chanock SJ, Caporaso NE, Ji BT, Weissfeld JL, Hayes RB. *CYP1A1 Val462* and *NQO1 Ser187* polymorphisms, cigarette use, and risk for colorectal adenoma. *Carcinogenesis* 2005; February 24 [Epub ahead of print])

ESOPHAGEAL CANCER

Tissue Zinc Levels and Cancer Risk

In rodents, zinc deficiency potentiates the effects of certain nitrosamines that act as esophageal carcinogens. The association between incident esophageal squamous cell carcinoma and zinc was examined using baseline esophageal biopsy specimens from residents of Linzhou, China participating in a nutrition intervention trial in this high-incidence area. X-ray fluorescence spectroscopy was used to measure zinc, copper, iron, nickel, and sulfur concentrations from biopsies collected in 1985 from 60 eventual case and 72 control subjects, matched on baseline histology and followed for 16 years. The risk of developing esophageal cancer was much lower for subjects in the highest quartile of esophageal tissue zinc concentration compared with those in the lowest quartile (hazard ratio [HR] = 0.21; CI = 0.065–0.68; *p* for trend = .015).

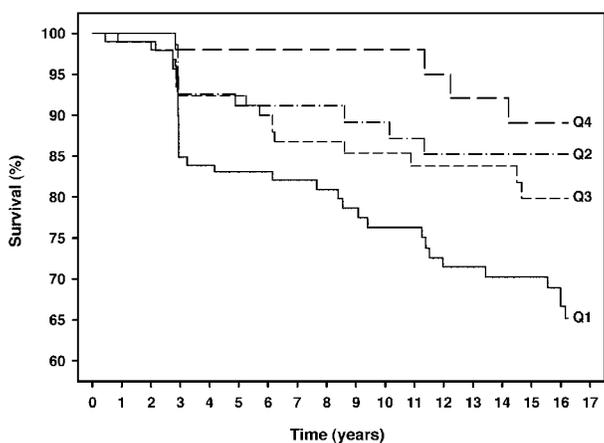


Figure 1. Percentage of incident esophageal squamous cell carcinoma-free survival among residents of Linzhou, China, according to quartile of baseline tissue zinc level. (Abnet CC, et al. 2005)

Individuals in the highest quartile of sulfur concentration also had a lower risk of esophageal cancer than those in the lowest quartile (HR = 0.29; CI = 0.095–0.85), but the trend was not significant (p for trend = 0.081) (Figure 1). There was no association between copper, iron, or nickel concentrations and risk of esophageal cancer. (Abnet CC, Lai B, Qiao YL, Vogt S, Luo XM, Taylor PR, Dong ZW, Mark SD, Dawsey SM. Zinc concentration in esophageal biopsy specimens measured by x-ray fluorescence and esophageal cancer risk. *J Natl Cancer Inst* 2005;97:301-306)

GASTRIC CANCER

Genetic Polymorphisms

A cross-sectional study compared prevalences of genetic polymorphisms among 302 subjects with mild chronic atrophic gastritis with prevalences in 606 subjects with deep intestinal metaplasia or dysplasia, selected from 2,628 individuals who had gastric biopsies in 1989 in Shandong Province, China. In subjects with mild chronic atrophic gastritis, the frequencies of the less common alleles of *CYP2E1 RsaI*, *CYP2E1 DraI*, *GSTP1*, *ALDH2*, and *ODC* were, respectively, 0.156, 0.201, 0.189, 0.190, and 0.428. The frequencies of the null genotypes of *GSTM1* and *GSTT1* in the group with mild chronic atrophic gastritis were 0.509 and 0.565, respectively. Interactions were noted between salt consumption and

GSTP1, between sour pancake consumption and *CYP2E1 RsaI*, and between *CYP2E1 DraI* and smoking at least one cigarette per day; a non-significant interaction between *CYP2E1 RsaI* and smoking status was noted. These polymorphisms do not seem to govern progression from mild chronic atrophic gastritis to advanced pre-cancerous gastric lesions,

but the effects of smoking may be accentuated in individuals carrying variants of *CYP2E1*. (You WC, Hong JY, Zhang L, Pan KF, Pee D, Li JY, Ma JL, Rothman N, Caporaso N, Fraumeni JF Jr, Xu GW, Gail MH. Genetic polymorphisms of *CYP2E1*, *GSTT1*, *GSTP1*, *GSTM1*, *ALDH2*, and *ODC* and the risk of advanced precancerous gastric lesions in a Chinese population. *Cancer Epidemiol Biomarkers Prev* 2005;14:451-458)

GENETICS

Effect of Electron-beam Irradiation

Electron-beam (E-beam) irradiation, currently used to sterilize mail addressed to selected ZIP codes in the United States, has significant negative effects on the genomic integrity of DNA extracted from buccal-cell washes. The authors investigated the yield, composition, and genotyping performance of whole genome amplified DNA (wgaDNA) derived from 24 matched samples of E-beam-irradiated and non-irradiated genomic DNA (gDNA) as a model for the effects of degraded gDNA on the performance of whole genome amplification. Compared with wgaDNA derived from non-irradiated gDNA, wgaDNA derived from irradiated gDNA exhibited a significantly reduced yield of wgaDNA and significantly reduced short tandem repeat and single nucleotide polymorphism genotyping completion and concordance rates ($p < 0.0001$). Increasing the amount of irradiated gDNA

input into whole genome amplification improved genotyping performance of wgaDNA but not to the level of wgaDNA derived from non-irradiated gDNA. Thus wgaDNA derived from E-beam-irradiated gDNA is not suitable for genotyping analysis. (Bergen AW, Qi Y, Haque KA, Welch RA, Garcia-Closas M, Chanock SJ, Vaught J, Castle PE. Effects of electron-beam irradiation on whole genome amplification.

Cancer Epidemiol Biomarkers Prev 2005;14:1016-1019)

Follow-up of Retinoblastoma Survivors

Many children who develop retinoblastoma (Rb) survive into adulthood and are prone to subsequent cancers, particularly persons with germline *Rb-1* mutations. The authors have extended the follow-up of 1,601 Rb patients, diagnosed during 1914–1984 at two U.S. medical centers, by seven years through the year 2000 to provide new information on the risk of cancers in long-term survivors. Subsequent cancer risk in 963 hereditary patients (standardized incidence ratio [SIR] = 19; CI = 16–21) exceeded the risk in 638 nonhereditary Rb patients (SIR = 1.2; CI = 0.7–2.0). Radiation further increased the risk of subsequent cancer in hereditary patients by 3.1-fold (CI = 2.0–5.3). Hereditary patients continued to be at increased risk for sarcomas, melanoma, and cancers of the brain and nasal cavities. The cumulative incidence for developing a new cancer at 50 years after diagnosis of Rb, adjusted for competing risk of death, was 36% (CI = 31%–41%) for hereditary and 5.7% (CI = 2.4%–11%) for non-hereditary patients (Figure 2, page 16). Hereditary Rb predisposes to a variety of new cancers over time, with radiotherapy further enhancing the risk of tumors arising in the radiation field. (Kleinerman RA, Tucker MA, Tarone RE, Abramson DH, Seddon JM, Stovall M, Li FP, Fraumeni JF Jr. Risk of new cancers after radiotherapy in long-term survivors of retinoblastoma: An extended follow-up. *J Clin Oncol* 2005;23:2272-2279)

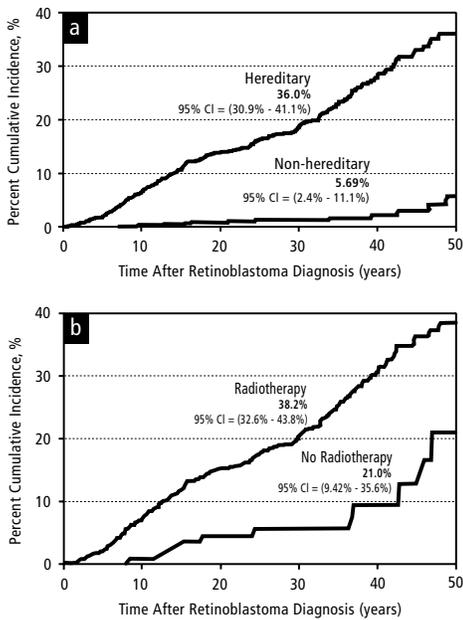


Figure 2. (a) Cumulative incidence and 95% CIs of new cancers by time since diagnosis of retinoblastoma by hereditary status; (b) Cumulative incidence and 95% CIs of new cancers by time since diagnosis of hereditary retinoblastoma by radiotherapy. (Kleinerman RA, et al. 2005)

KAPOSI SARCOMA

Genetic Susceptibility to Kaposi Sarcoma

Studies of *FCGR3A*, a gene expressed on natural killer cells, among men with HIV/AIDS suggest that host responses affect the pathogenesis of Kaposi sarcoma herpesvirus (KSHV) infection and risk of AIDS-related Kaposi sarcoma. Using DNA from two HIV seronegative case-control populations in Italy, relationships of the functional *FCGR3A*-V158F variant with risks of KSHV infection and classic Kaposi sarcoma (CKS) were examined. Overall, compared with the 158F allele, 158V was overrepresented among controls from both populations (frequency = 0.52 and 0.51, respectively). After controlling for age, 158V homozygous women were at increased risk of KSHV infection and CKS, compared with 158F homozygous women (OR = 8.7; CI = 0.8–98 and OR = 3.8; CI = 1.0–14, respectively), whereas 158V homozygous men were at decreased risk (OR = 0.4; CI = 0.1–2.3 and OR = 0.4; CI = 0.2–0.8, respectively). Significant gene-dose effects were observed among men and women

at risk for CKS (p for trend ≤ 0.05). Thus gender differences could possibly modify the effect of *FCGR3A* on risk of KSHV infection and CKS. (Brown EE, Fallin MD, Goedert JJ, Chen R, Whitby D, Foster CB, Lauria C, Alberg AJ, Messina A, Montella M, Rezza G, Vitale F, Chanock SJ. A common genetic variant in *FCGR3A*-V158F and risk of Kaposi sarcoma herpesvirus infection and classic Kaposi sarcoma. *Cancer Epidemiol Biomarkers Prev* 2005;14:633–637)

LIVER CANCER

Diabetes and Liver Cancer Risk

Diabetes has been associated with an increased risk of hepatocellular carcinoma (HCC), but U.S. population-based data are lacking. The Surveillance, Epidemiology, and End Results Program (SEER)-Medicare linked database was used to identify 2,061 patients aged 65 years and older diagnosed between 1994 and 1999 with HCC and 6,183 controls. Inpatient and outpatient claims files were searched for diagnoses of diabetes, hepatitis C virus (HCV), hepatitis B virus (HBV), alcoholic liver disease, and haemochromatosis. Compared with controls, patients with HCC were more often male (66% vs. 36%) and non-white (34% vs. 18%). Adjusting for demographics and other HCC risk factors (HCV, HBV, alcoholic liver disease, and haemochromatosis), diabetes was associated with a threefold increase in the risk of HCC. In a subset of patients without these major risk factors, the adjusted odds ratio for diabetes persisted (OR = 2.87; CI = 2.49–3.30). A significant positive interaction between HCV and diabetes was also detected. (Davila JA, Morgan RO, Shaib Y, McGlynn KA, El-Serag HB. Diabetes increases the risk of hepatocellular carcinoma in the United States: A population based case control study. *Gut* 2005;54:533–539)

Effects of Carcinogen-metabolizing and DNA Repair Genes

High rates of hepatocellular carcinoma (HCC) in The Gambia, West Africa, are associated with a high prevalence of chronic

hepatitis B virus infection and heavy aflatoxin exposure via groundnut consumption. The effects of genetic polymorphisms in carcinogen-metabolizing (*GSTM1*, *GSTT1*, *HYL1**2) and DNA repair (*XRCC1*) enzymes were examined in a hospital-based study of 216 incident cases and 408 controls. Although the prevalence of variant genotypes was generally low, the *GSTM1*-null genotype (OR = 2.45; CI = 1.21–4.95) and the heterozygote *XRCC1*-399 AG genotype (OR = 3.18; CI = 1.35–7.51) were significantly associated with HCC. The risk for HCC with null *GSTM1* was most prominent among those with the highest groundnut consumption (OR = 4.67; CI = 1.45–15.1). Among participants who had all three suspected aflatoxin-related high-risk genotypes, a significant 15-fold increased risk of HCC was observed (OR = 14.7; CI = 1.27–169). Thus genetic modulation of carcinogen metabolism and DNA repair may alter susceptibility to HCC, and these effects may be modified by environmental factors. (Kirk GD, Turner PC, Gong Y, Lesi OA, Mendy M, Goedert JJ, Hall AJ, Whittle H, Hainaut P, Montesano R, Wild CP. Hepatocellular carcinoma and polymorphisms in carcinogen-metabolizing and DNA repair enzymes in a population with aflatoxin exposure and hepatitis B virus endemicity. *Cancer Epidemiol Biomarkers Prev* 2005;14:373–379)

Intrahepatic Cholangiocarcinoma

The incidence of intrahepatic cholangiocarcinoma has been increasing in the United States. The Surveillance, Epidemiology, and End Results Program (SEER)-Medicare database was used to evaluate the prevalence of known risk factors for intrahepatic cholangiocarcinoma and explore other potential factors in a study of 625 cases, aged 65 years and older diagnosed between 1993 and 1999, and 90,834 controls. Cases were older than controls (78.7 vs. 76.5 years) and more likely to be male (48.3% vs. 36.8%), but the racial composition was similar. Several risk factors were

significantly more prevalent among cases, including nonspecific cirrhosis (OR = 27.2), alcoholic liver disease (OR = 7.4), hepatitis C virus infection (OR = 6.1), HIV infection (OR = 5.9), diabetes (OR = 2.0), and inflammatory bowel disease (OR = 2.3). (Shaib YH, El-Serag HB, Davila JA, Morgan R, McGlynn KA. Risk factors of intrahepatic cholangiocarcinoma in the United States: A case-control study. *Gastroenterology* 2005;128:620-626)

Selenium and Liver Cancer Risk

Selenium (Se) is an essential trace mineral with known anticarcinogenic properties in humans. A nested case-control study was conducted to compare the Se content in toenail clippings of 166 individuals (154 men, 12 women) with hepatocellular carcinoma (HCC) to 394 healthy controls (360 men, 34 women) in Haimen City, China, where HCC is a leading cause of mortality. Median toenail Se was lower for HCC cases than controls ($p = 0.03$). Odds ratios and 95% confidence intervals for HCC mortality by increasing quartile of toenail Se were 1.00 (reference), 0.58 (0.32–1.03), 0.83 (0.48–1.42), and 0.50 (0.28–0.90) (p for trend = 0.06). This inverse association appeared stronger among those who did not consume alcohol and among women. (Sakoda LC, Graubard BI, Evans AA, London WT, Lin WY, Shen FM, McGlynn KA. Toenail selenium and risk of hepatocellular carcinoma mortality in Haimen City, China. *Int J Cancer* 2005;115:618-624)

LUNG CANCER

Residential Radon Exposure

Underground miners exposed to high levels of radon have an excess risk of lung cancer. Residential exposure to radon is at much lower levels, and the risk of lung cancer with residential exposure is less clear. An analysis of pooled data on 3,662 cases and 4,966 controls from seven North American residential radon case-control studies, all of which used long-term alpha-track detectors to

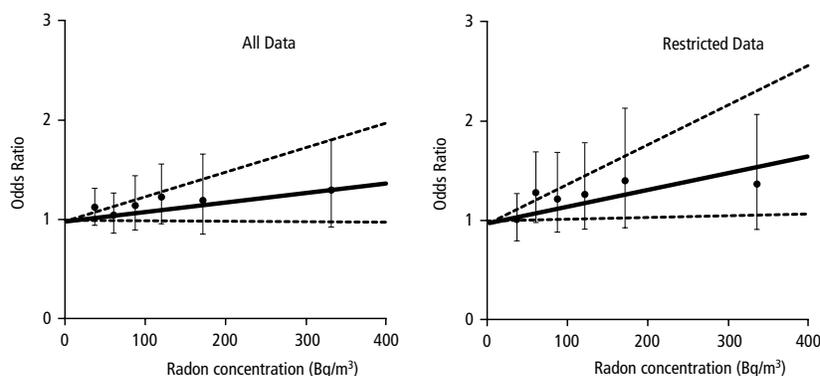


Figure 3. ORs and 95% CIs for categories of mean radon concentration within the 5- to 30-year exposure time window and the fitted model for the linear excess OR (solid line) and its 95% CI (dotted lines). (Krewski D, et al. 2005)

assess radon concentrations, was conducted. The estimated odds ratio after residential exposure to radon at a concentration of 100 Bq/m³ from 5 to 30 years before the index date was 1.11 (CI = 1.00–1.28). This estimate is compatible with the estimate of 1.12 (CI = 1.02–1.25) predicted by downward extrapolation of the miner data (Figure 3). Analyses restricted to subsets of the data with presumed more accurate radon dosimetry resulted in increased estimates of risk. (Krewski D, Lubin JH, Zielinski JM, Alavanja M, Catalan VS, Field RW, Klotz JB, Letourneau EG, Lynch CF, Lyon JI, Sandler DP, Schoenberg JB, Steck DJ, Stolwijk JA, Weinberg C, Wilcox HB. Residential radon and risk of lung cancer: A combined analysis of 7 North American case-control studies. *Epidemiology* 2005;16:137-145)

LYMPHOMA

Smoking and Non-Hodgkin Lymphoma

The International Lymphoma Epidemiology Consortium (InterLymph) provided an opportunity to analyze the relationship between cigarette smoking and non-Hodgkin lymphoma (NHL) with sufficient statistical power to consider NHL subtypes. In a pooled analysis of 6,594 cases and 8,892 controls from nine case-control studies conducted in the United States, Europe, and Australia, smoking was associated with a slightly increased NHL risk (OR = 1.07; CI = 1.00–1.15). Compared with nonsmokers,

current smokers had a higher odds ratio for follicular lymphoma (1.31; CI = 1.12–1.52) than former smokers (1.06; CI = 0.93–1.22). Current heavy smokers (≥ 36 pack-years) were associated with a 45% increased odds ratio for follicular lymphoma (1.45; CI = 1.15–1.82) compared with nonsmokers. Cigarette smoking may increase the risk of developing follicular lymphoma but not the other subtypes examined. (Morton LM, Hartge P, Holford TR, Holly EA, Chiu BC, Vineis P, Stagnaro E, Willett EV, Franceschi S, La Vecchia C, Hughes AM, Cozen W, Davis S, Severson RK, Bernstein L, Mayne ST, Dee FR, Cerhan JR, Zheng T. Cigarette smoking and risk of non-Hodgkin lymphoma: A pooled analysis from the International Lymphoma Epidemiology Consortium (InterLymph). *Cancer Epidemiol Biomarkers Prev* 2005;14:925-933)

METHODS

Adjustment for Nonresponse in Cohort Studies

Cohort studies often involve periodic follow-up interviews to determine disease incidence and to update measures of exposure. The practice of excluding nonrespondents from standardized incidence ratio (SIR) analyses can bias the outcome estimates if nonrespondents and respondents differ on important characteristics related to outcomes of interest. Thus, the authors proposed an analytic approach to reduce the impact of nonresponse in the analyses of SIRs.

Logistic regression models controlling for baseline information were used to estimate the probability of response; the reciprocals of these propensities were used as weights in the analysis of risk. This was illustrated in an analysis of 15 years of follow-up in a cohort of U.S. radiologic technologists who participated in an initial interview. Variances of the SIRs were estimated by a jackknife method that accounts for additional variability resulting from estimation of the weights, and results were robust to nonresponse. This method is flexible, easy to use with existing software, and applicable to missing data from cohorts with baseline information on all subjects. (Rao RS, Sigurdson AJ, Doody MM, Graubard BI. An application of a weighting method to adjust for nonresponse in standardized incidence ratio analysis of cohort studies. *Ann Epidemiol* 2005;15:129-136)

Gene-Environment Independence and Increased Power

Family-based case-control studies are often used to study the effects of genes and gene-environment interactions in the etiology of rare complex diseases. Herein, the authors considered methods for analyzing such studies assuming that genetic susceptibility (G) and environmental

exposures (E) are independently distributed within families in the source population. A novel conditional likelihood framework for exploiting the within-family G-E independence assumption was proposed, leading to a simple, highly efficient method of estimating interaction and other risk parameters. Moreover, the same paradigm led to even more efficient methods when parental genotype information was available. The relative efficiencies of different family-based and population-based designs were evaluated. Extensions of the methodologies for dealing with complex family studies were also discussed. (Chatterjee N, Kalaylioglu Z, Carroll RJ. Exploiting gene-environment independence in family-based case-control studies: Increased power for detecting associations, interactions and joint effects. *Genet Epidemiol* 2005;28:138-156)

PROSTATE CANCER

Vitamin E and Prostate Cancer Risk

The Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study demonstrated a 32% reduction in prostate cancer incidence in response to daily alpha-tocopherol supplementation. Baseline serum concentrations of alpha-tocopherol and gamma-tocopherol were

examined to compare their respective associations with prostate cancer risk among 100 randomly selected incident prostate cancer case patients and 200 control subjects in the ATBC Study cohort. Odds ratios for the highest versus the lowest tertiles were 0.49 (CI = 0.24–1.01; p for trend = 0.05) for alpha-tocopherol and 0.57 (CI = 0.31–1.06; p for trend = 0.08) for gamma-tocopherol. Further analyses indicated that the protective effect on prostate cancer risk was stronger in the alpha-tocopherol-supplemented group than in those not receiving alpha-tocopherol. (Weinstein SJ, Wright ME, Pietinen P, King I, Tan C, Taylor PR, Virtamo J, Albanes D. Serum alpha-tocopherol and gamma-tocopherol in relation to prostate cancer risk in a prospective study. *J Natl Cancer Inst* 2005;97:396-399)

UTERINE CORPUS CANCER

Clomiphene Citrate and Uterine Cancer Risk

Clomiphene citrate, a selective estrogen receptor modulator used to treat infertility, increases estradiol levels and therefore may increase risk of cancer of the uterine corpus. A retrospective cohort study was conducted of 8,431 women evaluated for infertility between 1965 and 1988 and followed through 1999. Clomiphene was associated with elevated uterine cancer risk ($n = 39$; rate ratio [RR] = 1.79; CI = 0.9–3.4), which increased further with dose (RR = 1.93; CI = 0.9–4.0 for > 900 mg), menstrual cycles of use (RR = 2.16; CI = 0.9–5.2 for ≥ 6 cycles), and time elapsed since initial use (RR = 2.50; CI = 0.9–7.2 for women followed for ≥ 20 years). Risk was more strongly associated among nulligravid (RR = 3.49; CI = 1.3–9.3) and obese (RR = 6.02; CI = 1.2–30.0) women, with risk substantially elevated among women who were both obese and nulligravid (RR = 12.52; CI = 1.5–108.0). (Althuis MD, Moghissi KS, Westhoff CL, Scoccia B, Lamb EJ, Lubin JH, Brinton LA. Uterine cancer after use of clomiphene citrate to induce ovulation. *Am J Epidemiol* 2005;161:607-615)



Wei-Cheng You with Joseph F. Fraumeni, Jr. (left) and Mitchell Gail (right).

VISIT FROM DIRECTOR OF BEIJING CANCER INSTITUTE

Dr. Wei-Cheng You, the Director of the Beijing Cancer Institute, arrived at DCEG in April for a month-long visit to work with **Mitchell Gail, M.D., Ph.D.**, and **Linda**

Morris Brown, Dr.P.H., members of the Biostatistics Branch, on the Shandong Intervention Trial (SIT). In 1995, Dr. You and NCI collaborators initiated a factorial randomized intervention trial in Linqu County, Shandong Province, to determine whether antibiotic treatment of *H. pylori*, vitamin supplements, or garlic supplements could reduce the prevalence of precancerous gastric lesions in this high-incidence population. The visit provided an opportunity for Dr. You and NCI staff to analyze data for the main end point of this seven-year trial. Dr. You also met with Division scientists to consider other possible studies based on data and resources of SIT. Dr. You was a DCEG fellow and principal investigator from 1991 to 2001 before returning to China to lead the Beijing Cancer Institute.

DCEG PEOPLE IN THE NEWS

Blanche Alter, M.D., M.P.H., Clinical Genetics Branch (CGB), discussed Fanconi anemia at the Stem Cell Transplantation in Children: Current Results and Controversies meeting in Scottsdale, Arizona in January. She also presented a case for a discussion on “Should patients be given research results?” at the NIH Ethics Grand Rounds in Bethesda, Maryland in April. She gave talks at the 5th Annual Diamond Blackfan Anemia International Conference in New York in April on “Cancer in Diamond-Blackfan anemia” and “Alternative therapies for Diamond-Blackfan anemia.” In addition, Dr. Alter spoke on “Etiologic investigation of cancer susceptibility in inherited bone marrow failure syndromes” at the American Society of Pediatric Hematology/Oncology Annual Meeting in Washington, DC in May.

Aaron Blair, Ph.D., Occupational and Environmental Epidemiology Branch (OEEB), gave an invited seminar on “Pesticides and human cancer” at the University of Washington in Seattle in February.

Melinda Butsch Kovacic, Ph.D., M.P.H., Hormonal and Reproductive Epidemiology Branch (HREB), in conjunction with science teachers, high school hatchling scientists, and other representatives of the American Junior Academy of Science, discussed her transition from laboratory researcher to epidemiologist working on cancer prevention at the annual meeting of the American Association for the Advancement of Science held at the NIH in February.



Kenneth Cantor

Kenneth Cantor, Ph.D. (OEEB), gave a talk on “Feasibility of conducting human studies to address bromate risks” at a workshop on research

strategies to study the health effects of bromate in drinking water at Miami University in Oxford, Ohio in February.

Several DCEG researchers recently received funding support from the NIH Office of Rare Diseases for workshops to develop international consortia related to familial chronic lymphocytic leukemia (**Neil Caporaso, M.D.**, Genetic Epidemiology Branch [GEB]), lymphoma (**Patricia Hartge, Sc.D.**, Epidemiology and Biostatistics Program [EBP]), and childhood cancer (**Martha Linet, M.D., M.P.H.**, Radiation Epidemiology Branch [REB]). Also supported were two research projects on dealing with renal cell cancer (**Lee Moore, Ph.D.** [OEEB] and **Jorge Toro, M.D.** [GEB]), AIDS-related malignancy (**Charles Rabkin, M.D.**, Viral Epidemiology Branch [VEB]), and cancer risk among ataxia-telangiectasia patients (**Ruth Kleinerman, M.P.H.** [REB]).

Philip Castle, Ph.D., M.P.H. (HREB), spoke at a meeting of the Cancer Council of the Pacific Islands on “The role of HPV

testing in cervical cancer screening” in Honolulu in March.

Mitchell Gail, M.D., Ph.D., Chief of the Biostatistics Branch (BB), gave an invited talk entitled “Criteria for evaluating models of absolute risk” at the Columbia University Department of Biostatistics in New York in March.

Several members of GEB participated in the 14th Genetic Analysis Workshop held in Noordwijkerhout, The Netherlands in September. **Lynn Goldin, Ph.D.**, **Alisa Goldstein, Ph.D.**, **Kimberly Kerstann, Ph.D.**, and **Rose Yang, Ph.D., M.P.H.**, along with **Andrew Bergen, Ph.D.**, Advanced Technology Center (ATC), and Kevin Jacobs (NCI contractor), contributed two papers: “Linkage analysis of GAW 14 simulated dataset with microsatellite and SNP markers in large pedigrees” and “Identification of susceptibility loci for complex diseases in a case-control association study of GAW 14 simulated dataset.”

MISSION TO HAITI

James Goedert, M.D., Chief of the Viral Epidemiology Branch, participated in a medical mission to Haiti from February 26 to March 6. His team of seven, including another physician, a nurse, and three others, traveled to the isolated community of Baraderes in rural southwest Haiti. They evaluated and provided basic medical care to 229 patients, arranged funding for 50 surgical procedures at a regional hospital, distributed toothbrushes and dental hygiene instruction to 850 students, and provided initial training to 16 high school students as future community health workers. Dr. Goedert observed extremely high rates of symptomatic, often disabling infection with *Helicobacter pylori*, intestinal helminthes, filariasis, and malaria. However, compared to 1995 when he participated in a similar mission to Baraderes, childhood malnutrition appeared to be less prevalent and less severe. His home church in Maryland currently sponsors a daily hot lunch, daily multivitamin, and thrice annual “worm pill” (albendazole) to 2,000 students in 13 affiliated schools.



James Goedert (front right) with newly trained community health students and associates of St. John Parish.

Ann Hsing, Ph.D. (HREB), was elected in March into the American Epidemiological Society, an honorary society of distinguished epidemiologists.



Jose Jeronimo

Jose Jeronimo, M.D. (HREB), who has recently been promoted from a Research Fellow to a Staff Scientist, spoke on “Diagnosis and treatment of HPV positive women” at a meeting of the Cancer Council of the Pacific Islands in Honolulu in March. In April, Dr. Jeronimo gave a Grand Rounds lecture at the School of Medicine of the University of California, Irvine.

Daehee Kang, M.D., Ph.D. (OEGB), gave talks on “Gene-environment interactions in breast cancer” at the National



Daehee Kang

Center for Toxicological Research in Little Rock in January; at Rutgers University in New Brunswick, New Jersey in March; and at the University

of Texas M.D. Anderson Cancer Center in April. He also co-chaired the Asian Cohort Consortium Meeting at the Fred Hutchinson Cancer Research Center in Seattle in April.

Joan Kramer, M.D. (CGB), has been promoted from Clinical Fellow to Staff Clinician.

Qing Lan, M.D., Ph.D. (OEGB), gave a talk on the “Use of intermediate endpoints to study the health effects of benzene” at the Johns Hopkins Bloomberg School of Public Health in March.

Maria Teresa Landi, M.D., Ph.D. (GEB), gave a presentation entitled “Known exposures, ‘unknown’ genes: Genetic epidemiology approaches to melanoma and lung cancer” at Stanford University in February.

Martha Linet, M.D., Chief of REB, spoke on “Childhood leukemia epidemiology: Etiology by subtype including translocations in fetuses” at the Radiation Effects Research Foundation in Hiroshima, Japan in February. She



Martha Linet

also gave a talk on “A cohort investigation of cancer and mortality risks in U.S. radiologic technologists: Opportunities for collaboration” at the National Institute of Environmental Health Sciences in Research Triangle Park, North Carolina in April.

Jennifer Loud, M.S.N., C.R.N.P. (CGB), was elected coordinator of the Cancer Genetics Special Interest Group for the Oncology Nursing Society for 2006.

Lee Moore, Ph.D. (OEGB), gave an invited speech on “Molecular epidemiological studies of cancer risk in human populations exposed to arsenic in drinking water” at the Penn State College of Medicine in May.



Lindsay Morton

Lindsay Morton, Ph.D. (HREB), who has been promoted from a CRTA Fellow to a Research Fellow, received an American Association for Cancer Research (AACR) Women in Cancer Research Brigid G. Leventhal Scholar Award in Cancer Research for her abstract on “Polymorphisms in the neurotransmitter reward and nicotine metabolism pathways in relation to smoking behavior in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial.” The award provided financial support for attendance at the 96th Annual AACR Meeting held in Anaheim, California in April. She has also been appointed as the DCEG co-representative to the NIH Fellows Committee.



Jay Nuckols

Jay Nuckols, Ph.D. (OEGB), gave a talk on “Exposure assessment for environmental epidemiology: Integrating earth and

NIH PLAIN LANGUAGE AWARDS

Publications by DCEG staff members won awards at the NIH fifth annual Plain Language Awards Ceremony, held April 27. Congratulations to **Michael Alavanja, Dr.P.H.**, Occupational and Environmental Epidemiology Branch, who coauthored an NCI/NIEHS booklet entitled “Cancer and the Environment: What You Need to Know, What You Can Do,” which received an Award of Excellence in the 2004 NIH Plain Language Award competition.

Kudos were also won by **Michele Doody, M.S.**, **Michal Freedman, Ph.D.**, **Martha Linet, M.D., M.P.H.**, **Elaine Ron, Ph.D.**, and **Alice Sigurdson, Ph.D.**, all members of the Radiation Epidemiology Branch (REB), along with Robert Weinstock, a contractor with REB, and Dr. Bruce Alexander and Ms. Diane Kampa, members of the University of Minnesota School of Public Health. Their newsletter on the U.S. Radiologic Technologists Study received an Honorable Mention in the competition.

NIH launched the Plain Language Initiative in 1999, following a White House memorandum calling for clearer writing throughout the federal government. Plain language documents should have logical organization and easy-to-read design features and use personal pronouns, short sentences, and common, everyday words.

—Sandy Rothschild

health sciences” at the State University of New York School of Public Health in Rensselaer in April.



June Peters

June Peters, M.S., C.G.C. (CGB), was one of three multi-credentialed faculty members to participate in the first interdisciplinary workshop on genetic

counseling and family therapy at the American Association of Marriage and Family Therapists Winter Institutes in Panama City, Florida in March.



Ruth Pfeiffer

Ruth Pfeiffer, Ph.D. (BB), gave an invited talk on “Criteria for evaluating models of absolute risk” at the Harvard School of Public Health in January.

Arthur Schatzkin, M.D., Dr.P.H., Chief of the Nutritional Epidemiology Branch (NEB), presented “Moving from observational studies to clinical trials: Why do we sometimes get it wrong?” at the NIH conference on Contribution of Biomarkers to Determining Causality in January.

Mark Sherman, M.D. (HREB), and **Diane Solomon, M.D.** (Division of Cancer Prevention and HREB), participated in a national teleconference on “Advances in cervical cancer screening” held in January. The broadcast was sponsored by the American Society of Cytopathology as part of a series that is viewed by cytotechnologists and pathologists throughout the country.

Alice Sigurdson, Ph.D. (REB), spoke on “Cancer and genetic susceptibility in the U.S. radiologic technologist cohort” at the Radiological and Biological Sciences Graduate Program at Colorado State University in Fort Collins in March.



Fan-Chen Tseng

Fan-Chen Tseng, Ph.D. (HREB), presented a poster on “The relationship of chronic HBV infection, chronic HCV infection and duration of injection drug use,” which was selected as a Poster of Distinction at the Digestive Disease Week meeting in Chicago in May.



Jim Vaught

Jim Vaught, Ph.D., Office of the Director (OD), Special Assistant for Biological Resources, spoke at the first European School of Haematology-European Blood and Marrow Transplantation Euroconference on Biobanking in Dublin in January. His presentation, “The International Society for Biological and Environmental Repositories,” summarized the history and goals of the organization, which was started in 1999 by NCI, CDC, and other scientists from government, academic, and commercial organizations.



Roel Vermeulen

Roel Vermeulen, Ph.D. (OEEB), gave a talk on “A study on immunological responses to exposures encountered in corn farming” at the Agricultural Health Study Biomarker Workshop on Cancer Etiology in Chapel Hill in March. He also gave a keynote address on “The *omics* era, what does it mean for industrial hygiene?” at the conference of the Dutch Association of Occupational Hygienists in Utrecht, The Netherlands in April.

Sholom Wacholder, Ph.D. (BB), spoke at the American Society of Preventive Oncology in San Francisco in March on



Sholom Wacholder

“Scaling up: Statistical issues in very large studies of genes and cancer.” The following week he delivered a paper titled “What is the chance that a negative report is a false negative?” at the American Epidemiological Society meeting in Baltimore.

Sophia Wang, Ph.D. (HREB), gave a talk titled “A molecular epidemiologist at 10 years: Results and applications in cervical cancer and lymphoma” at the Johns Hopkins Bloomberg School of Public Health.

Mary Ward, Ph.D. (OEEB), gave a talk on “Applications of GIS in cancer epidemiology studies” for GIS Day at State University of New York, Albany in April. GIS Day is a grassroots event that raises awareness of geographic information systems (GIS) technology.



Mingdong Zhang

Mingdong Zhang, M.D., Ph.D. (VEB), gave an invited talk on “Genetic susceptibility to human viral infections” at the Chinese University of Hong Kong in November.



Yawei Zhang

Yawei Zhang, M.D., Ph.D. (HREB), received an AACR Molecular Epidemiology Group Scholar-in-Training Award for her abstract titled “Polymorphisms in cell cycle pathway genes and risk of non-Hodgkin lymphoma.” The award defrayed travel expenses for attendance at the 96th Annual AACR Meeting held in Anaheim, California in April. Dr. Zhang’s abstract was also selected for presentation at a mini-symposium.

COMINGS . . . GOINGS

After more than four years serving as a Visiting Fellow in the Occupational and Environmental Epidemiology Branch (OEEB), **Juan Alguacil, M.D., Ph.D.**, has accepted a position at the University of Huelva in Spain. He will be leading the research unit on environmental and occupational epidemiology and teaching epidemiology, preventive medicine, and occupational and environmental health. During his stay with the OEEB, Dr. Alguacil made important contributions to the DCEG program, particularly in the areas of pancreatic cancer and bladder cancer epidemiology.

Yan Bai, M.D., Ph.D., a CRTA postdoctoral fellow with the Genetic Epidemiology Branch (GEB), has accepted a position in benefit risk management with Johnson and Johnson Pharmaceutical Research and Development in New Jersey.

Mark Donahue recently completed a three-year predoctoral fellowship in OEEB. Mr. Donahue has a bachelor's degree in history and science from Harvard College and spent his time at NCI learning epidemiological tools and performing statistical analyses for several Branch studies. He plans to pursue his interests in cancer in the health care industry.

Sadie Hutson, Ph.D., R.N., C.R.N.P., a postdoctoral fellow in the Clinical Genetics Branch (CGB), has accepted an Assistant Professor position in the

College of Nursing at East Tennessee State University in Johnson City. Dr. Hutson joined the CGB in 2002 and worked with **Blanche Alter, M.D., M.P.H.**, and **Mark Greene, M.D.**, to complete her thesis research on siblings of patients with Fanconi anemia.

Naoko Ishibe, Sc.D., joined GEB in 1997 as a postdoctoral fellow and later became a tenure-track investigator. Dr. Ishibe has accepted a position as a senior editor at the *Journal of the National Cancer Institute*.



Adrienne Katner

Adrienne Katner, M.S., has joined OEEB as a predoctoral fellow. Ms. Katner received an M.S. in environmental science from the University of Arizona, Tucson, in 1998. She is currently enrolled in the doctoral program in environmental science and engineering at the University of California, Los Angeles. She will be working on environmental exposure assessment in the multicenter case-control study of non-Hodgkin lymphoma.



Judy Lichaa

Judy Lichaa retired on March 31. Ms. Lichaa spent more than 15 years in the Division, working as a secretary in the Viral Epidemiology Branch

(VEB), the Office of the Director (OD), and OEEB. She plans to move to New Mexico to enjoy her retirement.

Annette Molinaro, Ph.D., a fellow in the Biostatistics Branch (BB) since June 2004, is taking a position as an Assistant Professor in the Division of Biostatistics at Yale University starting in July.

Charles Rabkin, M.D. (VEB), will be on sabbatical leave as a fellow-in-residence at Alfried Krupp College and a visiting professor in the Department of Hematology and Oncology at Ernst Moritz Arndt University in Greifswald, Germany from May through July.



José Reyes

José Reyes has joined CGB as a program assistant. He previously was a contract employee in BB.

Ana Cecilia Rodriguez, M.D., a longtime collaborator of the Hormonal and Reproductive Epidemiology Branch



Ana Cecilia Rodriguez

(HREB) from Costa Rica, has joined the Branch as a senior fellow under the auspices of the Oak Ridge Associated Universities Exchange Visitor Program. Dr. Rodriguez will be at DCEG for two years analyzing data from the Projecto Epidemiologico Guanacaste cervical cancer natural history study, which she helped direct. She will also continue to work on the field phase of the Human Papillomavirus Vaccine Trial.

Linda Ross has joined the Administrative Resource Center as the newest Administrative Officer. Ms. Ross was previously employed with the Substance



Tania Mara Welzel

WELZEL COMPLETES NIH/DUKE TRAINING

Tania Mara Welzel, M.D., Ph.D., M.H.S. (HREB), has successfully completed the NIH/Duke Training Program in Clinical Research. This two-year master's program, which is jointly offered by the Duke University School of Medicine and the NIH Warren G. Magnuson Clinical Center, provides academic training in the quantitative and methodological principles of clinical-epidemiological research. The program leads to a Master of Health Sciences degree, which is awarded by the School of Medicine at Duke University. Her thesis was entitled "Effect of HLA-B Bw4 and Bw6 alleles on risk for HIV transmission in heterosexual couples."



Linda Ross

Abuse and Mental Health Services Administration where she worked as a budget and program analyst. She will be supporting CGB and the Nutritional Epidemiology Branch (NEB).

Jennifer Rusiecki, Ph.D., a postdoctoral fellow in OEEB since 2002, has accepted a faculty position at the Uniformed Services University of the Health Sciences (USUHS) in Bethesda, Maryland. While at DCEG, she worked on the Agricultural Health Study, investigating associations between specific pesticide exposures and various cancers. She also worked on a spatial investigation of crop production in relation to prostate cancer and on studies involving biologic measurements of persistent organic pollutants. At USUHS, Dr. Rusiecki will work in the Preventive Medicine Department and teach a course in environmental and occupational epidemiology while continuing her research in these areas.



Fang Fang Zhang

Fang Fang Zhang, M.D., has joined the OEEB for a six-month predoctoral fellowship. Dr. Zhang received a medical degree from the Shanghai Medical University and is earning her Ph.D. from the Department of Epidemiology at Columbia University Mailman School of Public Health in New York. She will work with **Wong-Ho Chow, Ph.D.**, **Lifang Hou, M.D., Ph.D.**, and other investigators in DCEG analyzing genetic susceptibility and the effects of alcohol and folate in relation to stomach cancer risk.

PREVENTION RESEARCHERS JOIN DCEG

Philip Taylor, M.D., Sc.D., Nan Hu, M.D., Ph.D., Chaoyu Wang, M.S., and Luxia Qian, B.S., have transferred from the Center for Cancer Research (CCR) to GEB. Their research interests focus on developing cancer prevention strategies, particularly for cancers of the upper gastrointestinal tract. Dr. Taylor, senior investigator, received his medical degree from the University of Iowa in Iowa City in 1973 and completed his resi-



Philip Taylor, Luxia Qian, Nan Hu, and Chaoyu Wang.

idency in internal medicine at Vanderbilt University in Nashville, Tennessee in 1976. He joined the Centers for Disease Control in 1976 as an Epidemic Intelligence Services officer and while there completed a residency in preventive medicine. He received his master's and doctoral degrees in epidemiology from the Harvard School of Public Health and came to the NCI in 1983. Dr. Hu, staff scientist, received her medical degree from Shanxi Medical University in China in 1976, a doctorate in cancer genetics from Peking Union Medical College in Beijing, China in 1987, and an M.P.H. from George Washington University in Washington, DC in 1996. She has worked at the University of Chicago and the Chinese Academy of Medical Sciences and joined NCI in 1990. Mr. Wang, laboratory biologist, received his B.S. in cellular and molecular biology and genetics from the University of Maryland at College Park in 1997 and his M.S. in biotechnology from Johns Hopkins University in 2003. Dr. Hu and Mr. Wang will be located at the Molecular Epidemiology Laboratory Unit (MELU) at the Advanced Technology Center. Ms. Qian received her B.S. in statistics in 1988 and a certificate in biochemistry in 1991, both from Chengdu University in China. She recently was appointed to a technical position within the MELU through SAIC-Frederick, Inc.

Sanford Dawsey, M.D., Christian Abnet, Ph.D., M.P.H., Farin Kamangar, M.D., M.P.H., and Mark Roth, M.D., have transferred from CCR to join NEB. Their research interests include prevention and control of upper gastrointestinal cancers, particularly esophageal cancer. Dr. Dawsey, senior investigator, received his medical degree from Stanford University in 1976 and completed his residency in pathology at the University of Colorado in 1981 and a fellowship in cytology at the University of California, Los Angeles in 1987. He served as a pathologist at the McCormick Hospital in Chiang Mai, Thailand from 1982 to 1984 and at Saint Joseph Hospital in Denver, Colorado from 1984 to 1986. Dr. Dawsey joined NCI in 1987. Dr. Abnet, staff scientist, received his B.S. in biology from the University of Oregon in Eugene in 1989, a doctorate in environmental toxicology from the University of Wisconsin at Madison in 1998, and an M.P.H. from the University of Minnesota in Minneapolis in 1999. He joined NCI in 1998. Dr. Kamangar, a postdoctoral fellow, received his medical degree and an M.P.H. from Tehran University of Medical Sciences in Iran and an M.H.S. in biostatistics and Ph.D. in epidemiology from Johns Hopkins University. He joined NCI in 2001. Dr. Roth, staff clinician, received his B.S. degree from Dickinson College in Carlisle, Pennsylvania in 1987 and his medical degree from Temple University in Philadelphia in 1991. He came to the NCI in 1991 where he completed a pathology residency and a cytopathology fellowship.



Sanford Dawsey, Christian Abnet, Farin Kamangar, and Mark Roth.

TOWN MEETING WITH DCEG FELLOWS

In April, the DCEG Committee of Scientists (COS) sponsored the fifth annual DCEG Fellows' Town Meeting, which provided fellows with an opportunity to meet with the Division Director and other senior leadership to discuss aspects of the training program. Pre- and post-doctoral fellows were invited to raise issues that affect the quality of their training experience and career development while at DCEG. The meeting was coordinated by **Unhee Lim, Ph.D.**, Nutritional Epidemiology Branch, and **Jennifer Rusiecki, Ph.D.**, Occupational and Environmental Epidemiology Branch (OEEB)—COS Fellow Representatives working with the Women Scientists Advisors, **Lynn Goldin, Ph.D.**, Genetic Epidemiology Branch (GEB), and **Debra Silverman, Sc.D.** (OEEB).

This year, fellows heard reports from Dr. Lim and Dr. Rusiecki regarding actions that resulted from the 2004 meeting and issues raised in the 2004 COS Annual



Unhee Lim and Jennifer Rusiecki

Survey of DCEG Branch and Division Management. **Mary Lou McMaster, M.D.** (GEB), Chair of COS, provided an overview of the role of COS and expressed appreciation for the candid feedback on questions raised by fellows during previous meetings and annual surveys. **Joseph F. Fraumeni, Jr., M.D.**, Division Director, addressed policies for recruitment and retention of fellows and tenure-track investigators in conjunction with resource allocation and management,

as well as procedures related to content, timing, and dissemination of position announcements. Dr. Rusiecki teamed with **Shelia Zahm, Sc.D.**, Deputy Division Director, for a presentation on important considerations when negotiating for positions that follow fellowship training. **Demetrius Albanes, M.D.**, Chief of the Office of Education (OE), discussed the essential role of mentoring within DCEG and outlined plans for upcoming OE-sponsored workshops addressing critical elements of training and mentoring. **Robert Hoover, M.D., Sc.D.**, and **Patricia Hartge, Sc.D.**, Director and Deputy Director, respectively, of the Epidemiology and Biostatistics Program, contributed their own perspectives and insights to each of these discussions.

Following the presentations, the meeting shifted to a round-robin format, pairing two or more of the invited speakers with smaller groups of fellows for informal discussions. Participants were encouraged to raise topics of concern, offer candid feedback regarding their fellowship experience, and share ideas for improving the training program. COS will compile the issues raised and distribute the meeting minutes to all DCEG fellows. ■

—Mary Lou McMaster, M.D.,
Unhee Lim, Ph.D.,
and Jennifer Rusiecki, Ph.D.

DCEG TENURE-TRACK INVESTIGATOR RETREAT

DCEG held its second retreat for tenure-track investigators in April at the Rockwood Manor in Potomac, Maryland. Organized by **Shelia Zahm, Sc.D.**, Deputy Division Director, the program began with an overview by **Joseph F. Fraumeni, Jr., M.D.**, Division Director, who led the group in a discussion of the characteristics of NCI's Intramural Research Program, and of DCEG in particular, that allows the Division to conduct high-impact, high-quality science that is distinctive and "value-added" in nature. Dr. Barry Kramer, Office of the Director, NIH, shared his insights into how to craft a successful tenure package based on his experience with the NIH Central Tenure Committee as the chair of the NIH Epidemiology and Biometry Review Panel. Dr. Kramer's presentation was followed by a panel discussion on "Collaborations, Consortia, and Credit" with **Aaron Blair, Ph.D.**, Occupational and Environmental Epidemiology Branch, **Patricia Hartge, Sc.D.**, Epidemiology and Biostatistics Program (EBP), **Eric Engels, M.D., M.P.H.**, Viral Epidemiology Branch, and **Sophia Wang, Ph.D.**, Hormonal and Reproductive Epidemiology Branch. The panel reviewed the potential benefits and drawbacks of large-scale scientific collaborations for tenure-track investigators and presented strategies for demonstrating scientific independence and individual contributions to collaborative research projects. The retreat concluded with a question-and-answer session moderated by **Alice Sigurdson, Ph.D.**, Radiation Epidemiology Branch, in which Dr. Fraumeni and **Robert Hoover, M.D., Sc.D.** (EBP), responded to a series of "Myth or Truth?" statements concerning challenges facing tenure-track scientists as they carry out their research at NCI.

—Catherine McClave