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Division of Cancer Epidemiology and Genetics

Linkage

Celebrating DCEG's Tenth Anniversary, 1995–2005

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IN THIS ISSUE:

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DCEG Leads NCI Enterprise Initiative in Genomics

Capitalizing on the extraordinary momentum generated by advances in human genetic research, DCEG is forging ahead with one of the first major whole genome scanning projects in cancer. The Cancer Genetic Markers of Susceptibility (CGEMS) study will use the latest genetic technologies to perform dense whole genome scans. These scans will be used to identify and validate susceptibility genes for breast and prostate cancers and to clarify gene-gene and gene-environment interactions. This work will provide new insights into mechanisms of carcinogenesis and point the way to novel strategies for meeting the Director's 2015 Challenge Goal by accelerating the prevention, early detection, and treatment of cancer. This three-year NCI Enterprise Initiative project is a close collaboration of the NCI Core Genotyping Facility (CGF) and the NCI Office of Cancer Genomics, directed by Dr. Daniela Gerhard.

Previous linkage studies in families at high risk for developing cancer have successfully identified highly penetrant single genes that cause cancer at specific sites. These heritable syndromes have provided crucial insights into mechanisms of carcinogenesis such as cell-cycle control and DNA repair that, in turn, have provided important therapeutic leads. Despite these advances, highly penetrant cancer-causing mutations are uncommon in the general population and are responsible for only a small proportion of human cancer. Most human cancer risk is probably due in part to low-penetrant but common susceptibility alleles that remain to be identified. One of the main goals of CGEMS is to identify new genes that contribute to cancer risk. Dr. Hoover noted, "CGEMS is an attempt to let the genome tell us what is important; this truly is a different approach."

CGEMS will be led by **Stephen Chanock, M.D.,** Director of CGF; **Robert Hoover, M.D., Sc.D.,** Director of the Epidemiology and Biostatistics Program; and Dr. David Hunter, an NCI Eminent Scholar and the Vincent L. Gregory Professor of Cancer Prevention at the Harvard School of Public Health. **Gilles Thomas, M.D., Ph.D.,** who recently joined DCEG from the Fondation Jean Dausset Centre d'Etude du Polymorphisme Humain in Paris, France, will serve as the project's Scientific Director and lead geneticist. DCEG coinvestigators include **Richard Hayes, D.D.S., Ph.D.,** of the Occupational and Environmental Epidemiology Branch, **Sholom Wacholder, Ph.D.,** of the Biostatistics Branch, and **Joseph F. Fraumeni, Jr., M.D.,** DCEG Director. Project planning is currently under way, and the first genome scans are scheduled to commence in late 2005.

CGEMS Leaders: (front) Gilles Thomas and David Hunter; (back) Robert Hoover and Stephen Chanock.

DCEG *Linkage*

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Recent advances such as the sequencing of the human genome, the rapid progress in the National Human Genome Research Institute (NHGRI) International HapMap project, and the development of technologies for very large-scale single nucleotide polymorphism (SNP) genotyping now make it possible to execute well-designed association studies using common variants across the entire genome that map the low-penetrant genes most often involved in cancer susceptibility.

"The probability is that over the next three to five years, the field will be able to discover the genetic variants that contribute modest risk and fill in a piece of the cancer susceptibility puzzle not previously known."

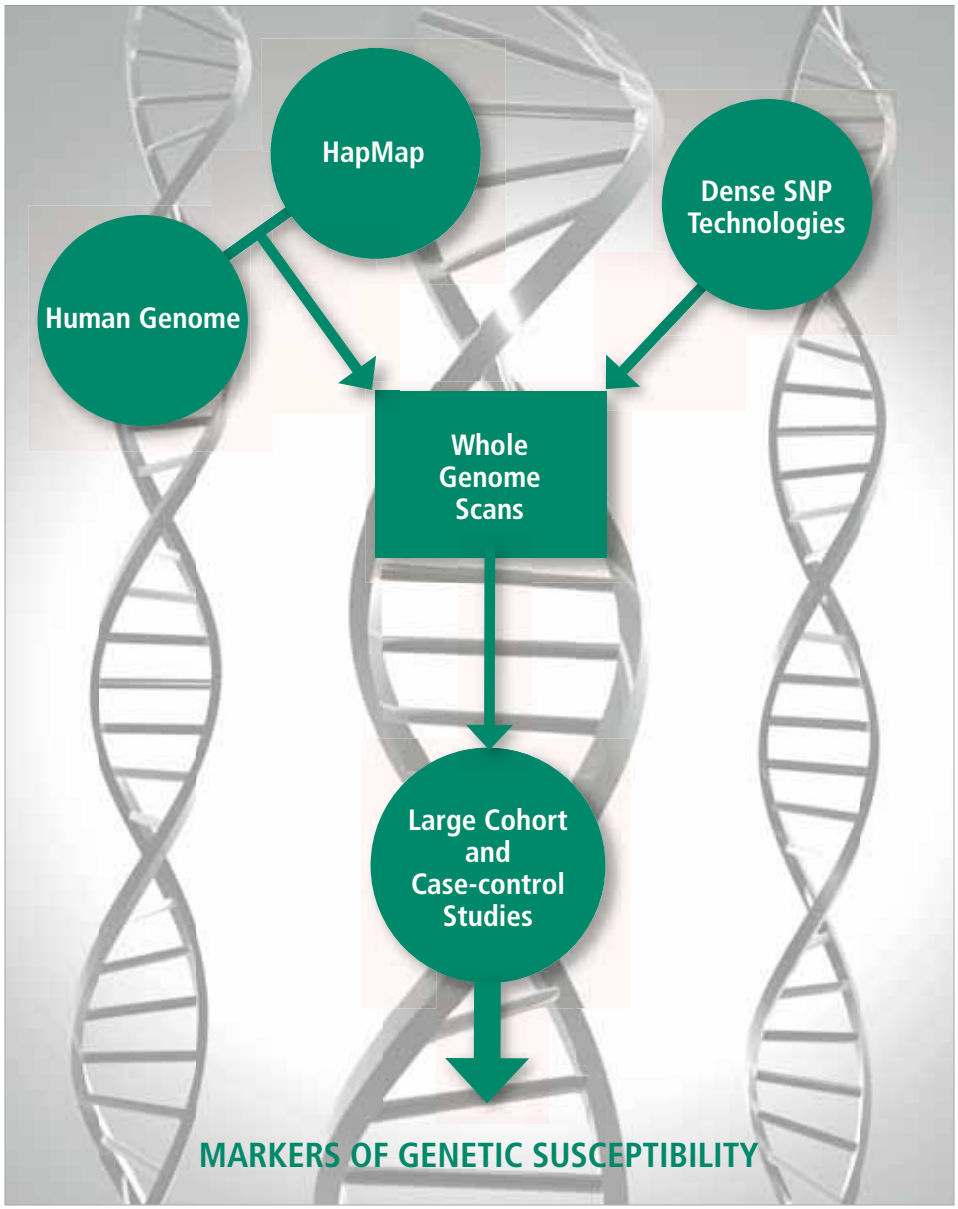
What makes CGEMS and other association studies different from candidate gene studies is that they "interrogate" the entire genome with no assumptions about which genes cause prostate and breast cancer. The markers used in identifying and mapping genetic variations are SNPs. Within the human genome, over 6 million common SNPs have been identified in which the minor allele occurs in more than 5% of the population. Due to the ancestral nature of patterns of linkage disequilibrium, select SNPs can serve as surrogate markers for others. Thus, a significantly smaller number of SNPs are needed in genomic studies, making whole genome scans feasible. "Previous technologies permitted the interrogation of only about 300 to 500 loci," Dr. Hunter commented. "But now, scientists are able to look at 300,000 to 500,000 loci in the genome, so there is much finer resolution." Coordination with NHGRI's International HapMap Consortium will help lay the groundwork to rapidly identify the panel of SNPs to be used in the genome scans.

Full genome scans will be conducted first on 1,200 prostate cancer patients and 1,200 controls and then on an equivalent number of breast cancer patients and controls. The associations identified in the whole genome scan require validation in subsequent studies in order to eliminate false positives and define regions of significance. One of the strengths of CGEMS is the plan for rapid, sequential replication in DCEG cohorts and case-control studies, as well as extramural cohort studies.

"The probability is that over the next three to five years, the field will be able to discover the genetic variants that contribute modest risk and fill in a piece of the cancer susceptibility puzzle not previously known," Dr. Hunter stated. "From there, scientists may go in different directions—they may make high-risk stratifications to identify groups of individuals that may need earlier or more frequent cancer screening; they may look into the fundamental mechanisms underlying the cancer process; or they may look more closely at the gene-environment interactions that are involved."

The biggest challenge facing the CGEMS team is handling the enormous amount of data produced by the initial genome

ERRATUM
In the July 2005 issue, page 3, the correct name for IMS is Information Management Services.



scans. Statistical and informatics expertise will play a key role in quickly analyzing the scan data, determining candidate genes to validate, conducting the secondary analyses, and making final datasets publicly available in a timely manner. A new database and informatics will be developed at the CGF for CGEMS and linked to the current Laboratory Information Management System for the sequential replication studies.

The findings from CGEMS will be made widely available as rapidly as possible. Researchers at NCI and throughout the extramural community will have access to the validated data on the internet via caBIG, the cancer Biomedical Informatics Grid. caBIG is an open-source, open-access, voluntary information network that will enable cancer researchers to share tools, standards, data, applications, and technologies according to common standards and needs. Researchers can also follow up with fine mapping, gene inclusion/exclusion, and functional and other studies to identify the underlying biologic mechanisms of cancer susceptibility. ■

—Alyssa Voss Minutillo, M.P.H.

TESTIFYING BEFORE CONGRESS

On May 25, **André Bouville, Ph.D.,** of the Radiation Epidemiology Branch (REB), testified before two groups in the U.S. House of Representatives about radiation dosimetry and cancer risk estimates for residents of the Republic of Marshall Islands (RMI) following the U.S. nuclear weapons testing in the 1950s. Dr. Bouville addressed the Committee on Resources and the Committee on International Relations (Subcommittee on East Asia and the Pacific). On July 18, **Kiyohiko Mabuchi, M.D., Dr.P.H.** (REB), testified on the same topic before the Senate Committee on Energy and Natural Resources. **Steve Simon, Ph.D.** (REB), testified at both hearings about his pre-NCI dosimetry research in the RMI. The NCI estimates were developed by a team from REB, which included Drs. Bouville, Mabuchi, and Simon, along with **Ethel Gilbert, Ph.D., Charles Land, Ph.D., Martha Linet, M.D., M.P.H.,** and **Elaine Ron, Ph.D.** For more information, go to http://dceg.cancer.gov/radia-researchDosimetryRMI.html.

—Betsy Duane-Potocki

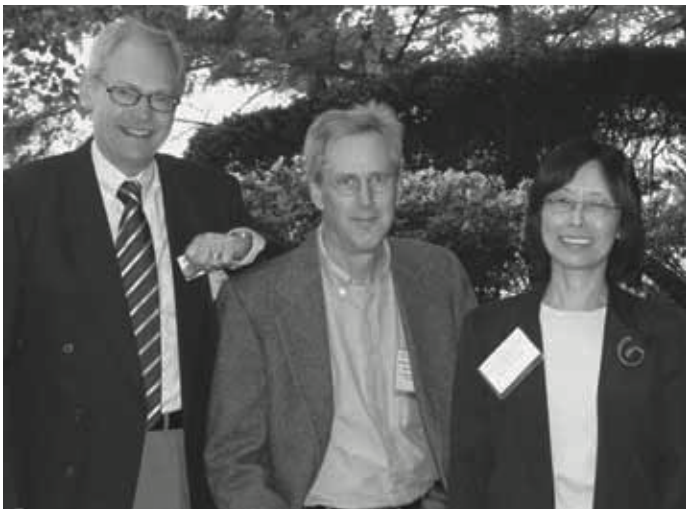
André Bouville (third from left at table) testifies before the House of Representatives.

BEACON: A NEW INTERNATIONAL CONSORTIUM

Incidence rates for esophageal adenocarcinoma (EA) have risen steeply in the United States and other Western countries during the past 30 years. Among white men in the United States, the increases have outpaced those for any other cancer, although rates have risen substantially in other groups as well.

Investigators have been able to identify a few moderately strong risk factors for EA and its precursor—Barrett's esophagus—including tobacco use, obesity, and gastroesophageal reflux. However, progress in research on this cancer has been limited. "Because this cancer has been relatively uncommon, many of the studies, at least the first-generation investigations, involved small numbers of subjects and an even smaller subset of subjects who provided biospecimens," said **Wong-Ho Chow, Ph.D.,** of the Occupational and Environmental Epidemiology Branch. One approach to surmounting the problem of small numbers is the formation of a consortium—a voluntary network of scientists who have agreed to cooperative research efforts to enable the sharing of ideas, data, tools, and specimens across population-based studies.

Building a foundation for the new Barrett's Esophagus and Adenocarcinoma Consortium (BEACON) was the topic of a workshop held at the NCI on May 9 and 10, 2005, with support provided by the NIH Office of Rare Diseases. Planned by Dr. Chow, Dr. Olof Nyrén of the Karolinska Institutet in Stockholm, and Dr. Thomas Vaughan of the Fred Hutchinson Cancer Research Center in Seattle, the workshop was attended by more than three dozen scientists from the United States, Europe, and Australia. It represented the start of collaborative efforts among researchers dedicated to the study of Barrett's esophagus and EA.



BEACON Workshop Planning Committee: Olof Nyrén, Thomas Vaughan, and Wong-Ho Chow.

One approach to surmounting the problem of small numbers is the formation of a consortium—a voluntary network of scientists who have agreed to cooperative research efforts to enable the sharing of ideas, data, tools, and specimens across population-based studies.

During the workshop, principal investigators from 14 separately funded case-control studies outlined the types of data and biospecimens available, described the status of ongoing and completed research, and identified possible avenues for collaborative work. Several laboratory and clinical investigators gave presentations on state-of-science research approaches that may be applied to these tumors. Dr. Daniela Seminara (Division of Cancer Control and Population Sciences) and Dr. Ernest Hawk (Division of Cancer Prevention) of NCI, as well as Dr. Frank Hamilton and Dr. Jay Everhart of the National Institute of Diabetes and Digestive and Kidney Diseases, provided information about possible sources of support for the consortium's activities. Some participants spoke about their experiences with other consortia. **Stephen Chanock, M.D.,** described the resources available through NCI's Core Genotyping Facility for high-throughput genotyping in support of BEACON's efforts.

The second day of the workshop was devoted to developing an organizational framework for BEACON, which will consist of four working groups and a steering committee. Plans were made to develop short-term, intermediate, and long-term projects. Consortium members agreed to communicate regularly by teleconference and other means before meeting again in the spring of 2006. ■

—Wong-Ho Chow, Ph.D.,
and Karen Eddleman

CAREERS IN EPIDEMIOLOGY SEMINAR

In May, DCEG held its fifth annual Careers in Epidemiology Seminar. This annual event is offered to help the approximately 75% of DCEG fellows who take positions outside of the Division at the end of their fellowships. Organized by **Shelia Hoar Zahm, Sc.D.,** DCEG Deputy Director, the series of seminars involves DCEG alumni, who inform fellows of opportunities in other settings and offer practical advice on how to find and negotiate for these jobs. This year's speakers were Dr. Allen E. Bale, Associate Professor of Genetics and Director of the DNA Diagnostic Laboratory and the Cancer Genetics Program at Yale University School of Medicine; Dr. Ahmedin Jemal, Department of Epidemiology and Surveillance Research, American Cancer Society (ACS); and Dr. Deborah M. Winn, Chief of the Clinical and Genetic Epidemiology Research Branch, NCI Division of Cancer Control and Population Sciences (DCCPS).

During his years at NCI, Dr. Bale received training in genetics and epidemiology in DCEG as well as in the Laboratory of Biochemistry in the Center for Cancer Research. He spoke to the fellows on the challenges and rewards of shaping an interdisciplinary research program. He encouraged them to establish a research area that they could develop further as a junior faculty member and to identify and pursue the type of job they want. When considering a position, he advised them to ensure that the institution has the type of core facilities they would need, to compare graduate and medical schools in terms of tenure requirements and access to students, and to evaluate all aspects of start-up packages including salary; benefits; number of years of "protected time" for research; and funds for supplies, equipment, and personnel. He stressed the importance of keeping focused on the work needed to be successful.

Dr. Jemal has continued the descriptive epidemiology research in which he trained at DCEG in his work on cancer surveillance activities at ACS. The ACS tracks cancer incidence, mortality, and survival, as well as trends in cancer risk factors and use of screening tests. Dr. Jemal's annual reports on U.S. cancer statistics are among the most frequently cited papers in biomedical journals. He described the power of descriptive epidemiology to generate interesting clues to cancer etiology and the development of new statistical methods to increase the accuracy of projections.

After Dr. Winn's postdoctoral fellowship in DCEG, she worked at the National Center for Health Statistics and the National Institute of Dental and Craniofacial Research before returning to NCI as Program Director and Branch Chief in DCCPS. Each of these positions enhanced her scientific, technical, and practical skills. She described the satisfaction a program director can enjoy from working with extramural investigators to foster their research, helping to move cancer epidemiology forward by contributing to the scientific agenda in cancer epidemiology, identifying priorities for the Institute, developing infrastructure, and participating in team science and research consortia. She emphasized that leading and participating in scientific teams is a key and growing part of cancer epidemiology. She encouraged the fellows to take full advantage of the various types of training opportunities available to them, including topics such as media training.

Fellows can also find many useful references on career development, interviewing, negotiating, scientific management, and mentoring in the DCEG Office of Education library, located outside EPS 3048 and organized by **Kristin Kiser, M.H.A.** ■

—Shelia Hoar Zahm, Sc.D.

Ahmedin Jemal, Allen Bale, and Deborah Winn with Shelia Zahm.

SPRING 2005 INTRAMURAL RESEARCH AWARDS

To provide more competitive funding opportunities for fellows and tenure-track scientists and to encourage innovative, interdisciplinary research, DCEG recently expanded its Intramural Research Award (IRA) program to include a spring and fall cycle. In each cycle, up to three proposals will be funded.

The winners of the spring 2005 competition are **James Lacey, Ph.D.,** of the Hormonal and Reproductive Epidemiology Branch (HREB), for his proposal on "*PTEN* tumor suppressor gene alterations in the progression from endometrial hyperplasia to carcinoma"; **Ola Landgren, M.D., Ph.D.,** of the Genetic Epidemiology Branch, for his project on "Familial, epidemiologic, and biologic features of monoclonal gammopathy of underdetermined significance"; and **Lindsay Morton, Ph.D.** (HREB), for her proposal entitled "Defining molecular subtypes of lymphoma for relevance to etiology, diagnosis, and survival."

The IRA proposals were reviewed by members of the NCI Board of Scientific Counselors or other extramural scientists with appropriate expertise, along with senior DCEG scientists. The proposals were judged with respect to their potential for significant scientific or public health impact, innovative aspects of approach or methodology, interdisciplinary or collaborative nature, ability to achieve the objectives within the proposed time frame and resources, and programmatic relevance to Division and Institute priorities. ■

Intramural Research Award Winners: James Lacey, Lindsay Morton, and Ola Landgren.

—Sandy Rothschild

ANNUAL SURVEY OF BRANCH AND DIVISION MANAGEMENT

The DCEG Committee of Scientists (COS) conducts an annual survey of Branch and Division management that is critical to maintaining an optimal research environment. COS was created in 1995 to identify and promote practices that enhance scientific life in the Division and to advise the DCEG Director on issues such as communication, removing administrative obstacles to productive research, and career development. Following its inception, COS immediately recognized a need for a bidirectional approach to performance review, since the success of DCEG's mission depends not only on the productivity of the scientific staff but also on the management skills and practices at the Branch and Division levels. The DCEG Annual Survey of Branch and Division Management was the product of that early COS vision.

The annual survey is designed to allow staff an opportunity to provide candid assessment of issues that affect Branch and Division management and to suggest constructive approaches to enhance the scientific environment in DCEG. Many of the issues raised in a recent survey (e.g., how to attract and retain a scientific staff of distinction, how to improve management of shared Division resources during times of budget constraints) formed the agenda for extended discussion at a Senior Advisory Group Retreat, while several other issues were targeted for action in ensuing months. Survey results are an important part of the Division Director's annual human resource planning meetings with Branch Chiefs.

The survey has become an essential component of the ongoing dialogue between Division leadership and staff, who are devoted to achieving the DCEG vision of scientific excellence.

COS employs several strategies to protect the confidentiality of staff members, such as delinking responses from each participant's e-mail address and position. Only the Division Director and Deputy Director view verbatim comments pertaining to Branch management, while the COS chair also reviews responses that address Division-wide issues. Because the survey is essentially a management tool, not a typical epidemiologic data collection instrument, COS has increasingly used open-ended questions designed to elicit narrative comments. COS representatives welcome content and formatting suggestions as well as questions about any facet of the survey (http://intranet.dceg.cancer.gov/committees/cos/cosmembers). The survey has become an essential component of the ongoing dialogue between Division leadership and staff, who are devoted to achieving the DCEG vision of scientific excellence.

—Mary Lou McMaster, M.D.

DCEG PROBES NON-PARTICIPATION IN EPIDEMIOLOGIC STUDIES

Non-participation appears to be a growing problem in the field of epidemiology, threatening confidence in research results. At the recent Joint Meeting of the Society for Epidemiologic Research (SER) and the Canadian Society for Epidemiology and Biostatistics in Toronto, **Patricia Hartge, Sc.D.,** Deputy Director of the Epidemiology and Biostatistics Program, organized and spoke at a scientific session dedicated to the issue. In her talk, "How big is the problem and what is the solution?" she said, "Epidemiologists must consider the effect of non-participation on self-selection and misclassification bias in our studies, not only during analysis and publication, but also at the earliest stages of study design and implementation."

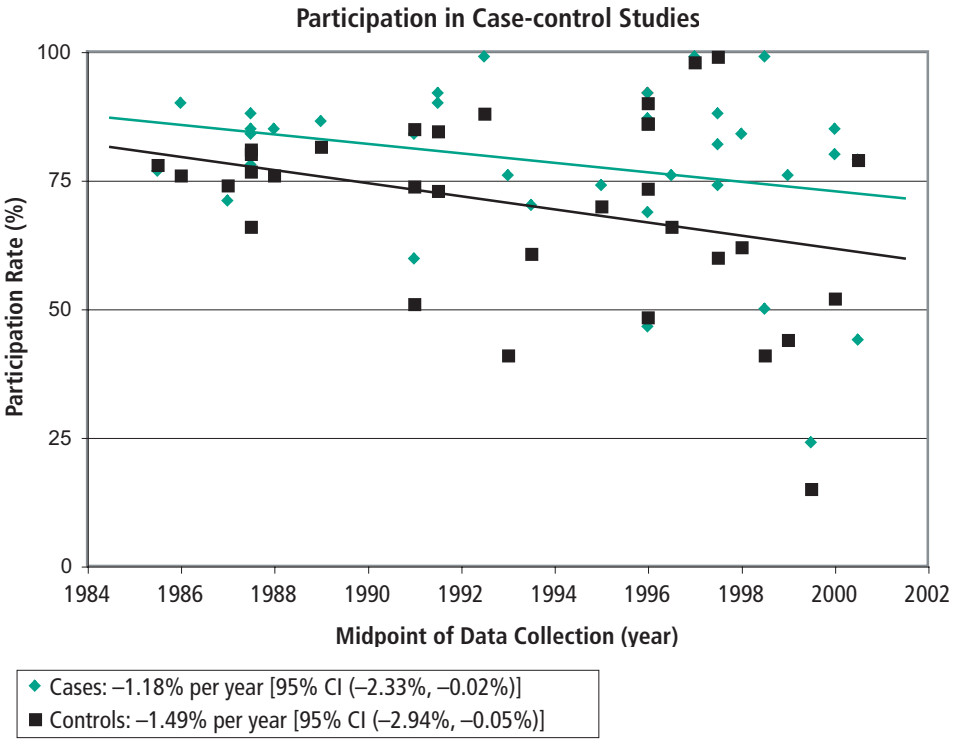


Figure 1: Decline in participation rates in case-control studies. (Morton L, et al., in press)

Meeting attendees learned about the related work of two DCEG fellows, **Lindsay Morton, Ph.D.,** of the Hormonal and Reproductive Epidemiology Branch, and **Jinbo Chen, Ph.D.,** of the Biostatistics Branch. Dr. Morton submitted a poster on her survey of current reporting practices for epidemiologic studies begun between 1970 and 2003. She found that a surprising proportion of published studies in epidemiology journals did not report any information about subject participation rates, making it difficult for scientists to assess and address the extent of the phenomenon across the field, especially at a time when biospecimen collections are more frequently a component of participation. "More troubling," according to Dr. Morton, "is our discovery that in those studies reporting sufficient or any response information, participation rates have been declining for all study designs (see Figure 1). The sharpest declines occurred within the last decade, especially in case-control studies and particularly in population control subjects."

In a session on "Bias: Methodological and practical considerations," Dr. Chen presented her biostatistical analysis entitled, "Quantifying selection bias in epidemiologic studies," which showed that in case-control studies, the ratio of exposed and non-exposed cases and controls who are non-responsive, rather than simply the overall level of non-response, determines the extent of bias.

In related work, the first study to look at the relationship between genetics and non-response was conducted by **Parveen Bhatti, M.S.,** of the Radiation Epidemiology Branch (REB). Mr. Bhatti analyzed single nucleotide polymorphism genotypes, haplotypes, and short tandem repeats (STRs) among control groups from three DCEG studies. Among 2,955 individuals, he compared 108 genotypes, 8 haplotypes, and 9 to 15 STRs by respondent type. He concluded that "there was little evidence to suggest that genetic characteristics relate to willingness to respond," adding, "This was just the first set of genes examined."

The summary of Dr. Hartge's session will appear as a commentary in an upcoming issue of *Epidemiology*. Dr. Morton's study will appear in the *American Journal of Epidemiology*; Dr. Chen's will be submitted later this year; and Mr. Bhatti's research will appear in *Cancer Epidemiology, Biomarkers & Prevention*. In addition, **Cecile Ronckers, Ph.D.** (REB), identified factors affecting questionnaire response in a cohort study published in the *Annals of Epidemiology* in 2004. ■

—Alyssa Voss Minutillo, M.P.H.

BIOSPECIMEN COLLECTION WORKSHOP

NCI hosted a workshop from July 18 to 20 on "Best practices for establishing and maintaining biorepositories that support cancer research." The workshop was the second in a series organized by the NCI Biospecimen Coordinating Committee (BCC). The first meeting, which concerned ethical, legal, and policy issues relevant to NCI biorepositories, was held from June 23 to 24. The workshops shared an overall mission of identifying and recommending best practices for the establishment and maintenance of human biospecimen repositories designed to broadly support cancer research and development.

The July workshop was chaired by Dr. Anna Barker, NCI Deputy Director for Advanced Technologies and Strategic Partnerships, and Dr. Mark Rubin of the Dana-Farber Cancer Institute. **Jim Vaught, Ph.D.,** DCEG Office of the Director (OD), and Dr. Julie Schneider, NCI OD, co-chaired the BCC subcommittee that developed the workshop agenda. **Marianne Henderson, M.S.,** Chief of the DCEG Office of Division Operations and Analysis, also served on the BCC subcommittee. **Neil Caporaso, M.D.,** of the Genetic Epidemiology Branch, **Montserrat Garcia-Closas, M.D., Dr.P.H.,** of the Hormonal and Reproductive Epidemiology Branch, **Patricia Hartge, Sc.D.,** Deputy Director of the Epidemiology and Biostatistics Program (EBP), and **Robert Hoover, M.D., Sc.D.,** Director of EBP, were among the more than 100 workshop participants.

In her opening remarks, Dr. Barker noted that biospecimens represent the future of personalized medicine. NCI's biorepositories support not only individual investigators, but also many of the NCI's strategic initiatives, including:

- The NCI cancer Biomedical Informatics Grid (caBIG);
- A national clinical proteomics technology initiative to provide common infrastructure and standardization;
- A forthcoming collaborative pilot program with the National Human Genome Research Institute to lay the groundwork for sequencing cancer genomes;
- The Alliance for Nanotechnology in Cancer to catalyze development of technologies and products that can interact with and interrogate cells for diagnosis and treatment.

The workshop agenda addressed biorepository practices from several perspectives, including basic, population, and clinical sciences, as well as the patient's perspective. Plenary sessions addressed cross-cutting issues, such as quality control and bioinformatics, as well as the variety of analytical methods applied to biorepository specimens.

The first of two working group sessions addressed best practices according to specimen type (blood, tissue, and other) as well as bioinformatics and quality control/quality assurance practices. The second working group session addressed a new proposal for evaluating and monitoring the quality of NCI biorepositories. The working group reports highlighted many areas of agreement on best biorepository practices and called for additional research into unresolved issues, such as optimal specimen collection methods that maximize stability for different types of laboratory analyses.

Recommendations developed by the workshop discussions were presented in September to the National Cancer Advisory Board and will be made available for public comment later in the year. In June, Dr. Carolyn Compton joined NCI as the Director of Biorepositories and Biospecimen Research. She will establish a biorepository science research program to follow up on these recommendations. ■

—Marianne Henderson, M.S., and Jim Vaught, Ph.D.

Workshop Organizers: (front) Jim Vaught and Julie Schneider; (back) Carolyn Compton and Anna Barker.

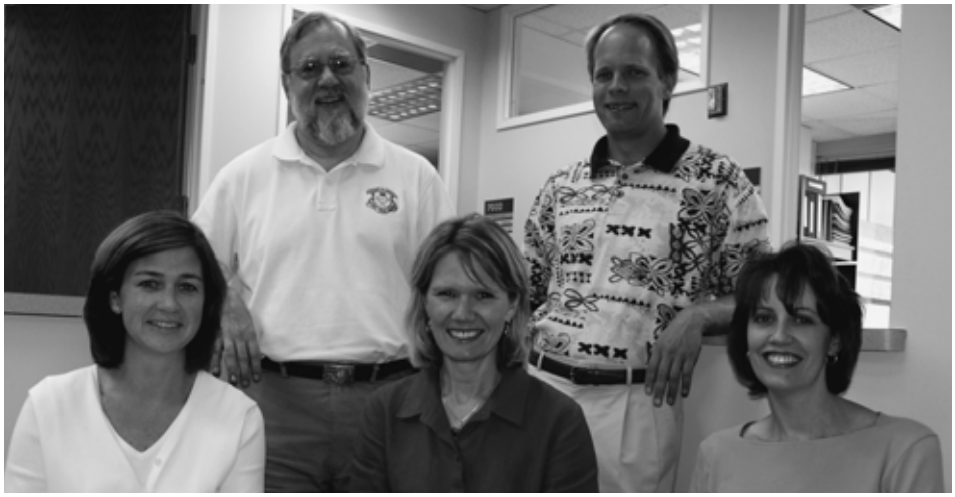
FAIR-EM: A NEW MANAGEMENT SYSTEM FOR FAMILY STUDIES

Computerized study management systems are an integral part of conducting clinical research protocols in the Clinical Genetics Branch (CGB) and the Genetic Epidemiology Branch (GEB). The Family and Individual Registry Event Management (FAIR-EM) System provides a secure Web interface that allows users to track the status of study subjects' day-to-day study-related events and information as they move through the pre-clinic, clinic, post-clinic, and follow-up phases of a study. Investigators from CGB and GEB, working with contractors from Information Management Services, Inc., and Westat, Inc., designed a tool that can be inexpensively and quickly adapted to the data collection and clinic scheduling requirements of any new study. Although FAIR-EM was designed with the needs of family studies research in mind, the system template is adaptable to other types of studies as well.

Each study within the current system has its own set of participant and event data fields and system-enforced rules for determining participant enrollment and event eligibility. Users may add, update, and view the status of each subject's completion of study events. When a defined event status is modified, the system generates and/or modifies other events for that participant as specified for the study. FAIR-EM users may search for participants and events through an interface that includes all database fields within a study. The interface allows users to choose which fields they want displayed in the search results.

One of the most important features of this system is interactive data entry, which provides an efficient and accurate means to monitor all aspects of data collection. The resulting computer files generated from the study management system facilitate rapid, up-to-date report generation. Study events and their outcomes are scheduled and recorded in accordance with each study's standard operating procedures. The events that are typically monitored using FAIR-EM include:

- Recruitment phone calls and letters;
- Status of informed consent;
- Scheduling of clinic visits;
- Acquisition of biological specimens;
- Performance of study-related tests and procedures;
- Completion of questionnaires and other data collection instruments;
- Requests for medical records and pathology;
- Mailing of participant "thank you" letters.



FAIR-EM Development Team: (front) Beth Mittl, Jennifer Loud, and Susan Pfeiffer; (back) Mark Greene and Kevin Meagher (Not shown: Ruth Foelber, Joan Kramer, and Sheila Prindiville).

Reports can include the number of participants who are active, completed, or withdrawn from a study; the number of participants who have been evaluated; the number of follow-up studies required; and the number of adverse events that have occurred to participants in a study.

Each study schedule records interim and final disposition for each individual participant. Triggers and rules that are specific to a study schedule help determine the individuals who are eligible for each study step. This process identifies patients who need to be scheduled for future encounters and helps users keep track of each protocol-related component as it is completed.

Administrative reports provide information on events that are outstanding and stages that are anticipated in the near future. Summary reports allow the study team to monitor the progress of the study by viewing event statistics across the cohort or in cohort sub-groups. These reports also provide information required by study monitoring agencies and institutional review boards (IRBs).

FAIR-EM was initially implemented to support CGB's Breast Imaging study and then modified for use in the Familial Testicular Cancer project. This conversion was accomplished at a fraction of the time and cost that would have been required to build a new study management tool *de novo*. FAIR-EM can be adapted to meet changing study requirements and for new studies quickly, efficiently, and at a relatively low cost. For further details, see the DCEG Tools Web site at http://dceg.cancer.gov/tools_study.html. ■

—Jennifer Loud, M.S.N., C.R.N.P., and Mark Greene, M.D.

RUTH PFEIFFER ADDS POWER TO GENETIC STUDIES

A problem solver by nature, tenure-track investigator **Ruth Pfeiffer, Ph.D.,** of the Biostatistics Branch (BB), works closely with other researchers at DCEG, the Karolinska Institute in Stockholm, George Washington University, Mulago Hospital in Kampala, Uganda, and elsewhere.

"I like to work with people to find solutions to challenging scientific problems," she said. "My passion for problem solving probably comes from my engineering background." The results of her collaborations and innovative statistical approaches have led to important findings—some of which have run counter to widely accepted thinking.

Dr. Pfeiffer earned a master's degree in applied mathematics (computer science) in her native country of Austria. She came to the United States when she received a Fulbright Fellowship to study applied statistics in 1992–1993, and she subsequently earned a doctorate in mathematical statistics from the University of Maryland in 1998. She recalled, "When I took a summer course on statistical genetics at the University of North Carolina, I really became interested in biological applications. The genome project was starting to yield a tremendous amount of genetic information. I wanted to work with genetic data, because I knew it would open up a world of research opportunities." She joined the NCI as a fellow in 1999 and became a tenure-track investigator in 2001.

One major focus of Dr. Pfeiffer's research is genetic epidemiology. Jointly with **Mitchell Gail, M.D., Ph.D.,** Chief of BB, she developed a random effects model to analyze family-based studies of cancer and assess associations with environmental and genetic factors while accounting for data ascertainment and

Ruth Pfeiffer

different familial correlations. After showing that the model was reasonably robust, she applied it to a wide variety of datasets.

One example is a family study of nasopharyngeal cancer in Taiwan with **Allan Hildesheim, Ph.D.,** of the Hormonal and Reproductive Epidemiology Branch (HREB). The study is investigating associations with consumption of salted fish during childhood and other exposures as well as genetic factors. Dr. Pfeiffer has also teamed up with **Maria Teresa Landi, M.D., Ph.D.,** of the Genetic Epidemiology Branch (GEB), and extended the random effects model, combining family and case-control data to analyze the effects of variants in the melanocortin 1 receptor *(MC1R)* gene on melanoma risk.

"It was a challenge to combine these two types of data," Dr. Pfeiffer said. "But this approach greatly increased the power of the study." In a study with Dr. Bert Zbar of the Center for Cancer Research (CCR), she is currently assessing risk factors in families with renal cancer.

The random effects model can be used for a surprisingly wide range of problems. Working with Dr. Louise Ryan of Harvard University, Dr. Pfeiffer devised a longitudinal case-cohort design utilizing the same type of model. Currently, she is comparing the random effects model with other ways of analyzing family data.

Dr. Pfeiffer has devised survival methods to detect familial aggregations of cancer using record-linkage data from Sweden and Denmark. Databases describing familial relationships are linked to national cancer registries and are often performed as a preliminary step to case-control or family-based studies. As Dr. Pfeiffer observed, "Aggregation of cancer in families provides an important clue that a genetic or environmental factor is at work." In a collaborative effort with **Lynn Goldin, Ph.D.** (GEB), and researchers at the Karolinska Institute, she demonstrated significant familial aggregation of Hodgkin lymphoma and chronic lymphocytic leukemia, and she is examining the familial risks of other cancers associated with these cancers.

Dr. Pfeiffer and **Sarah Daugherty, M.P.H.,** a predoctoral fellow in the Occupational and Environmental Epidemiology Branch, made a startling discovery attempting to detect "anticipation" of non-Hodgkin lymphoma. "Anticipation means that a disease with a genetic component has successively younger ages of onset as it gets passed from generation to generation." According to Dr. Pfeiffer, anticipation "only has a proven molecular mechanism in Huntington's disease," but the phenomenon had been reported for non-Hodgkin lymphoma in some studies. "By applying survival methods and correcting for secular trends, such as increasing incidence in the population, the anticipation effects disappeared." Those findings led to a paper published

in *Cancer Epidemiology, Biomarkers & Prevention.* "The take-home lesson is that if the incidence of a condition changes in the population, then one must control carefully for those changes before interpreting effects based on age-of-onset data."

Dr. Pfeiffer is particularly proud of a finding that arose from another major research focus—models for studying viral disease. She works closely with **Sam Mbulaiteye, M.D.,** of the Viral Epidemiology Branch, whose interest is human herpesvirus 8 (HHV-8), the causative agent of Kaposi sarcoma. "This virus is very interesting," Dr. Pfeiffer said. "Its prevalence in Western countries is low except in patients with acquired immunodeficiency syndrome, but in Sub-Saharan Africa, it is endemic. However, exact modes of transmission are not well understood."

There is some evidence that HHV-8 is blood-borne, which would help spread the disease to children with sickle cell anemia because they receive many transfusions. Using Dr. Mbulaiteye's cross-sectional data on the transfusion histories of those children, Dr. Pfeiffer built a Markov model and was able to estimate the probability per transfusion of becoming infected with HHV-8, even though the serology data were collected at a single point in time. The model, which allows for interchild heterogeneity in susceptibility to infection, indicated that the risk of HHV-8 infection was about 2.6% per transfusion.

What lies ahead for Dr. Pfeiffer? Her newest challenge lies in the field of high-dimensional molecular data, such as proteomics data that may be useful in the early detection of cancer. However, no standard statistical approaches to analyzing these data exist. She has been collaborating with Dr. Efstathia Bura of George Washington University on applying and extending dimension reduction and inverse regression techniques to analyze these data. When she looks to the future, Dr. Pfeiffer foresees even greater reliance on molecular data to address epidemiologic problems. "We will also have to learn more about causal pathways to discern interactions between the environment and genetic factors in the development of cancer."

One thing is clear: DCEG is where she wants to continue her work: "This is a fantastic research environment! I'm extremely lucky to be here." ■

—Karen Eddleman

MIA GAUDET RECEIVES SALLIE ROSEN KAPLAN FELLOWSHIP

Mia Gaudet, Ph.D., joined the Hormonal and Reproductive Epidemiology Branch (HREB) in July as DCEG's first recipient of the Sallie Rosen Kaplan (SRK) Fellowship for Women Scientists in Cancer Research, a competitive program for new women postdoctoral fellows applying to train in NCI's Intramural Research Program. The Foundation for the National Institutes of Health provides the endowment for the fellowship based on a bequest from Ms. Kaplan, who was committed to the education and the professional enhancement of women. The fellowship is awarded annually to encourage talented young women scientists to pursue advanced training in cancer research and reward them for demonstrated excellence in their chosen field. SRK fellows receive augmented stipends.

Mia Gaudet

Dr. Gaudet, who holds a doctoral degree in epidemiology from the University of North Carolina at Chapel Hill, is collaborating with **Louise Brinton, Ph.D.** (Chief of HREB), **Montserrat Garcia-Closas, M.D., Dr.P.H.** (HREB), and **James Lacey, Ph.D.** (HREB). Dr. Gaudet was first exposed to DCEG while serving as a summer research intern with the Nutritional Epidemiology Branch four years ago. "As I became more familiar with the work and accomplishments of DCEG scientists, it strengthened my conviction to come here when I finished my doctorate," she said.

Dr. Gaudet is investigating a variety of biochemical and molecular markers in breast and other hormonally related cancers and their relationships to body mass index and physical activity. Studying these types of cancers is particularly compelling, according to Dr. Gaudet: "From a public health standpoint, although we understand some of the risk factors, as yet there is no 'smoking gun' like there is for tobacco smoking and lung cancer. That's why I am intrigued with hormonally related cancers."

Because she holds a bachelor's degree in nutrition and has investigated the role of nutrition in health and disease, Dr. Gaudet hopes to draw upon her background as she investigates the dietary and nutritional determinants of cancer. "One of my goals as a postdoctoral fellow," she said, "is to bring together all these etiologic components: genetics, hormones, and diet." Specifically, she is interested in gene-nutrient interactions and the interplay between nutrition and endogenic hormones in cancer prevention and control.

More information about the fellowship is available from the Foundation for NIH through its web site (www.fnih.org).

—Karen Eddleman

DCEG SUMMER FELLOWSHIPS

Every summer brings the prospect of introducing cancer epidemiology, genetics, and biostatistics research to a new cadre of bright and energetic students. This summer 20 students at academic levels ranging from high school through graduate school conducted research under the guidance of DCEG mentors.

"I am always impressed with the knowledge, enthusiasm, and energy the summer fellows bring to our research program. The posters clearly document the scientific contributions made by the fellows."

The Fifth Annual DCEG Summer Poster Session was held on August 5 with 13 students presenting posters to a standing-room-only crowd of DCEG staff. The students enjoyed discussing their projects with DCEG scientists, who offered relevant critiques and comments. A senior investigator in the Occupational and Environmental Epidemiology Branch (OEEB) and summer mentor, **Aaron Blair, Ph.D.,** said, "I am always impressed with the knowledge, enthusiasm, and energy the summer fellows bring to our research program. The posters clearly document the scientific contributions made by the fellows." Many of the students had presented to a large audience at the NIH-wide Summer Poster Session the day before. Several noted that getting recognition and feedback from those with experience and authority in their specific research area made the DCEG event both more challenging and more rewarding.

The poster session was preceded by an awards ceremony and discussion with **Joseph F. Fraumeni, Jr., M.D.,** DCEG Director, **Shelia Hoar Zahm, Sc.D.,** DCEG Deputy Director, and **Demetrius Albanes, M.D.,** Chief of the Office of Education and Senior Investigator in the Nutritional Epidemiology Branch.

Reflecting on her experience, University of Maryland graduate student **Lindsay Hoskins** said, "Working in the Clinical Genetics Branch (CGB) over the past several months has solidified my interest in continued work in the medical and biobehavioral field, specifically with regard to familial cancers. My summer experience has made me more aware of the challenges and opportunities that exist within this exciting new field."

This year DCEG hosted two participants in the highly competitive NCI Introduction to Cancer Research Careers (ICRC) program, **Sheila Thomas**, a master's

Research Projects by the 2005 Summer Fellows

Hereditary leiomyomatosis and renal cancer in relation to mutations in the fumarate hydratase gene. **Eitan Bernstein,** Charles E. Smith Jewish Day School. Mentors: **Jorge Toro, M.D.,** and **Ousmane Toure, Ph.D.** (both in GEB)

Elevated risk of lung cancer in people with HIV/AIDS in the United States. **Leonard Chang,** Montclair State University. Mentor: **Eric Engels, M.D., M.P.H.** (VEB)

HHV-8 viral and antibody profiles in patients with Kaposi's sarcoma in Uganda. **Susan Combs,** Oxford University. Mentor: **Sam Mbulaiteye, M.D.** (VEB)

Differential gene expression in gastric cardia cancer: Comparison of two methods. **Erica Dawsey,** University of Michigan. Mentors: **Philip Taylor, M.D.,** and **Nan Hu, M.D., M.P.H.** (both in GEB)

Using a geographic information system to evaluate environmental exposures to solvent releases and risk of non-Hodgkin lymphoma. **Hozefa Divan,** University of California, Los Angeles. Mentor: **Mary Ward, Ph.D.** (OEEB)

Tobacco use and health behaviors among a cohort of adult survivors of retinoblastoma. **Meredith Foster,** Wellesley College. Mentor: **Ruth Kleinerman, M.P.H.** (REB)

Immunophenotypic and clinical protein features of monoclonal B-cell lymphocytosis in unaffected relatives from B-CLL kindreds. **Shannon Gnall,** University of North Carolina at Chapel Hill. Mentor: **Neil Caporaso, M.D.** (GEB)

Changes in serum DDT/DDE levels between 1976 and 1998 among women from Triana, Alabama in relation to body mass index, parity, breastfeeding, and other factors. **Julia Gray,** University of Michigan. Mentor: **Aaron Blair, Ph.D.** (OEEB)

Utility of the colored eco-genetic relationship map for assessing social functioning of women in HBOC families. **Lindsey Hoskins,** University of Maryland. Mentor: **June Peters, M.S., C.G.C.** (CGB)

Merkel cell carcinoma and multiple primary cancers. **Regan Howard,** George Washington University. Mentor: **Lois Travis, M.D., Sc.D.** (REB)

student in nursing education at Clemson University, and **Alexis Lebron**, a junior majoring in cell biology and genetics at the University of Maryland. ICRC offers students from diverse and/or disadvantaged backgrounds an opportunity to work at NCI for a summer; the awards also include support for summer housing and travel. ICRC participants are carefully selected by a committee of NCI principal investigators. For further details, see the ICRC web site (http://icrc.nci.nih.gov).

DCEG summer students with Shelia Zahm, Joseph F. Fraumeni, Jr., Demetrius Albanes, Kristin Kiser, and students' mentors. *(Photograph Credit: Mindy Kaufman)*

Summer student **Regan Howard** observed, "I thought the summer experience was a great chance to apply some of the principles that I've learned in school towards a specific project in a great research environment." Ms. Howard is in her second year in the M.P.H. program at George Washington University School of Public Health and Health Services.

Summer applications begin trickling in during the month of November and become a deluge of interested students from February through the end of May. Students interested in applying for the summer program are encouraged to view the DCEG Summer Web page (http://www.dceg.cancer.gov/summer.html), complete the summary application, and submit a full application to the NIH Summer Application site (http://www.training.nih.gov/student/index.asp), indicating their interest in epidemiology at NCI. DCEG received nearly 250 applications this year and accepted 20 students, a proportion similar to the NIH average. ■

—Kristin Kiser, M.H.A.

Analysis of 1-carbon metabolism in the Spanish Bladder Cancer study. **Sara Karami,** George Washington University. Mentor: **Lee Moore, Ph.D.** (OEEB)

The NCI dyskeratosis congenita cohort. **Sara Khaghani,** University of California, Los Angeles. Mentors: **Blanche Alter, M.D., M.P.H.,** and **Neelam Giri, M.D.** (both in CGB)

Increased non-Hodgkin lymphoma risk in association with family history of hematopoietic malignancies. **Zhao Elizabeth Lan,** Churchill High School. Mentor: **Sophia Wang, Ph.D.** (HREB)

Association of the CYP17 MspA1 gene polymorphism with prostate cancer in the ATBC study. **Alexis Lebron,** University of Maryland. Mentors: **Demetrius Albanes, M.D.,** and **Margaret Wright, Ph.D.** (both in NEB)

Association of smoking and oral lesions with HHV-8 in the U.S. population. **Luis Lee,** Ponce School of Medicine. Mentor: **James Goedert, M.D.** (VEB)

Physical activity in relation to all-cause mortality in the U.S. Radiologic Technologists study. **Sharifa Love-Schnur,** Yale University. Mentor: **Michal Freedman, Ph.D.** (REB)

MBL2 haplotypes and clearance of hepatitis C among injection drug users. **Rebecca Pass,** Stanford University. Mentors: **Thomas O'Brien, M.D., M.P.H.** (HREB), and **Beth Brown, Ph.D.** (VEB)

Human papillomavirus research from the laboratory to the clinic to population studies. **Jo Pretorius,** University of San Diego. Mentor: **Mark Schiffman, M.D., M.P.H.** (HREB)

Patient and health care provider education materials related to the management of menopausal symptoms in women who have undergone risk-reducing salpingo-oophorectomy. **Sheila Thomas,** Clemson University. Mentor: **Jennifer Loud, M.S.N., C.R.N.P.** (CGB)

Assessing the chance that the finding of a report is false. **Li Zhang,** University of Florida. Mentors: **Sholom Wacholder, Ph.D.,** and **Nilanjan Chatterjee, Ph.D.** (both in BB)

WALDENSTRÖM'S MACROGLOBULINEMIA NEWSLETTER

When **Mary Lou McMaster, M.D.,** Genetic Epidemiology Branch (GEB), wanted to communicate with participants in her family study of Waldenström macroglobulinemia (WM), she faced the singular challenge of explaining medical terms to a mixed audience of knowledgeable patients as well as others who may know much less about the disease. So she developed a highly effective newsletter that informs study participants about the disease and fosters the conduct of the research.

WM is a rare cancer that arises from B-lymphocytes (a type of white blood cell) that produce excess amounts of a very large protein called IgM. Because of its huge size, the excess IgM in the bloodstream makes the blood viscous, or sticky, leading to such symptoms as visual problems, nosebleeds, headaches, mental confusion, and rarely, stroke. Based on data from the NCI Surveillance, Epidemiology, and End Results (SEER) program, Dr. McMaster estimates that about 1,100 new cases of WM are diagnosed in the United States annually. Although only 12 WM families had been described worldwide since 1960, about 80 WM families (including over 170 WM patients and nearly 450 healthy relatives) have been identified and enrolled in the DCEG study since it began in 2001.


Waldenström's Macroglobulinemia Family Study
Newsletter

The DCEG family study of WM is designed to provide insights into the clinical spectrum of WM when it clusters in families and to identify genetic factors that contribute to susceptibility. "In general, WM patients are incredibly well-informed about their disease," said Dr. McMaster. "When I see a WM patient in the clinic, I am often seeing someone who knows more about the disorder than most physicians, and I have the time to explain our study methods and rationale using a variety of strategies designed to meet individual needs." Dr. McMaster communicates by letter, telephone, and face-to-face with family members who come to the NIH Clinical Center, although not all participants are able to travel to Bethesda for evaluation. "It is much more challenging to explain scientific and medical concepts about WM and genetic research methods to healthy relatives of WM patients," she said, "because—unlike many WM patients—family members may not be aware of, or have access to, other sources of information."

To meet this need, Dr. McMaster designed a newsletter to be distributed to all study participants. "I wanted to provide all our family members, regardless of their level of background knowledge, a working vocabulary for family and genetic studies in general, and WM in particular. The newsletter provides me another option to educate our families about some of the basic scientific concepts behind our work, to address frequently asked questions, to provide links to other sources of information, and to continue to express our appreciation for their contribution to WM research." In addition, each newsletter contains a postage-paid information form that allows participants to update their individual or family information, ask questions, and air concerns. Following the institutional review board approval, approximately 1,000 newsletters were sent out in May. "The response has been fantastic," said Dr. McMaster, after receiving more than 380 update forms during the first eight weeks following the mail-out. "Participant feedback has been overwhelmingly positive, and we have the added bonus of receiving some questions and comments that will help guide future issues of the newsletter." ■


Elizabeth Lobb and Nina Hallowell

GENETIC COUNSELING RESEARCH SEMINAR

In June, the Clinical Genetics Branch co-sponsored a special joint DCEG/Division of Cancer Control and Population Sciences seminar entitled "Cancer genetic counseling research: Psychosocial and practice issues" with presentations by several international speakers. Dr. Elizabeth Lobb from the University of Sydney spoke on risk communication, the genetic counseling process, and content analysis; Dr. Nina Hallowell of the University of Edinburgh presented a synopsis of her publications on lay understanding of risk, women's responses to risk communications, and decision-making regarding prophylactic surgery for hereditary breast-ovarian cancer.

SCIENTIFIC HIGHLIGHTS

ALL CANCERS

Infertility and Cancer

In a retrospective cohort study of 12,193 U.S. women evaluated for infertility between 1965 and 1988, 581 cases of cancer were identified through 1999. Infertility patients demonstrated a higher cancer risk than the general population (standardized incidence ratio [SIR] = 1.23; CI = 1.1–1.3), with nulligravid (primary infertility) patients at even higher risk (SIR = 1.43; CI = 1.3–1.6). Particularly elevated risks among primary infertility patients were observed for cancers of the uterus (SIR = 1.93) and ovaries (SIR = 2.73). Analyses within the cohort revealed increased rate ratios (RRs) of colon, ovarian, and thyroid cancers and of melanomas associated with endometriosis. Melanomas were linked with anovulatory problems, whereas uterine cancers predominated among patients with tubal disorders. Endometriosis was linked with distinctive excesses of cancers of the colon (RR = 2.40; CI = 0.7–8.4), ovaries (RR = 2.88; CI = 1.2–7.1), and thyroid (RR = 4.65; CI = 0.8–25.6), as well as melanomas (RR = 2.32; CI = 0.8–6.7). Primary infertility due to anovulation particularly predisposed to uterine cancer (RR = 2.42; CI = 1.0–5.8). The effects of infertility may extend beyond gynecologic cancers. Thyroid cancers and melanomas deserve specific attention, particularly with respect to endometriosis. **(Brinton LA, Westhoff CL, Scoccia B, Lamb EJ, Althuis MD, Mabie JE, Moghissi KS. Causes of infertility as predictors of subsequent cancer risk. *Epidemiology* 2005;16:500–507)**

BILIARY TRACT CANCER

Aspirin Use

The associations of gallbladder and bile duct cancers with gallstones, cholecystitis, and cholangitis suggest that chronic inflammation contributes to the carcinogenic process. A population-based case-control study conducted in Shanghai, China, examined the relationship between aspirin use and the risk of biliary disease among 627 patients with biliary tract cancer, 1,037 patients with biliary stones, and 958 healthy adults. Aspirin use was associated with a reduced risk of gallbladder cancer (odds ratio [OR] = 0.37; CI = 0.17–0.88), and an inverse relationship was observed with frequency and duration of use and use starting at a younger age. In addition, there were non-significant reductions in the risk of bile duct (OR = 0.48; CI = 0.19–1.19) and ampullary cancers (OR = 0.22; CI = 0.03–1.65) associated with aspirin use, whereas no clear association was seen with biliary stones (OR = 0.92; CI = 0.59–1.44). **(Liu E, Sakoda LC, Gao YT, Rashid A, Shen MC, Wang BS, Deng J, Han TQ, Zhang BH, Fraumeni JF Jr, Hsing AW. Aspirin use and risk of biliary tract cancer: A population-based study in Shanghai, China. *Cancer Epidemiol Biomarkers Prev* 2005;14:1315–1318)**

BLADDER CANCER

NAT2 and *GSTM1* Genes

The authors investigated polymorphisms in *NAT2, GSTM1, NAT1, GSTT1, GSTM3,* and *GSTP1* in 1,150 patients with transitional-cell carcinoma of the urinary bladder and 1,149 controls in Spain, and carried out meta-analyses that included over twice the numbers of cases in previous reports. The odds ratios for bladder cancer for individuals with deletion of one or two copies of the *GSTM1* gene were 1.2 (CI = 0.8–1.7) and 1.9 (CI = 1.4–2.7), respectively. Compared with *NAT2* rapid or intermediate acetylators, *NAT2* slow acetylators had an increased overall risk of bladder cancer (OR = 1.4; CI = 1.2–1.7) that was stronger for cigarette smokers than for never smokers (p for interaction = 0.008). No significant associations were found with the other polymorphisms. Meta-analyses showed that the overall association for *NAT2* was robust ($p <$ 0.0001), and case-only meta-analyses provided support for an interaction between *NAT2* and smoking (p for interaction = 0.009). The overall association for *GSTM1* was also robust ($p < 0.0001$) and was not modified by smoking status ($p = 0.86$). The *GSTM1* null genotype increases the overall risk of bladder cancer, and the *NAT2* slow-acetylator genotype also increases risk, particularly among cigarette smokers. Although the relative risks are modest, these polymorphisms could account for up to 31% of bladder cancers because of their high prevalence. **(García-Closas M, Malats N, Silverman D, Dosemeci M, Kogevinas M, Hein DW, Tardon A, Serra C, Carrato A, Garcia-Closas R, Lloreta J, Castaño-Vinyals G, Yeager M, Welch R, Chanock S, Chatterjee N, Wacholder S, Samanic C, Torà M, Fernández F, Real FX, Rothman N. *NAT2* slow acetylation, *GSTM1* null genotype, and risk of bladder cancer: Results from the Spanish Bladder Cancer study and meta-analyses. *Lancet* 2005;366:649–659)**

BREAST CANCER

Ataxia-Telangiectasia

Epidemiological studies have consistently shown elevated rates of breast cancer among female blood relatives of patients with ataxia-telangiectasia (AT), a rare autosomal recessive disease. A large proportion of the members of AT families are carriers of AT-causing gene mutations in *ATM*, and it has been hypothesized that these otherwise healthy carriers are predisposed to breast cancer. In a follow-up study of 1,445 blood relatives of 75 patients with verified AT in 66 Nordic families, 225 cases of cancer were identified through population registries, with 170.4 expected (SIR = 1.3; CI = 1.1–1.4). Invasive breast cancer occurred among 34 female relatives (SIR = 1.7; CI = 1.2–2.4) and was diagnosed among 21 women before the age of 55 years

(SIR = 2.9; CI = 1.8–4.5), including seven mothers of probands (SIR = 8.1; CI = 3.3–17). When the group of mothers was excluded, no clear relationship was observed between the allocated mutation carrier probability of each family member and the extent of breast cancer risk. The findings of breast cancer risk in mothers, but not other likely mutation carriers, in this and other studies raise questions about the hypothesis of a simple causal relationship with *ATM* heterozygosity. **(Olsen JH, Hahnemann JM, Borresen-Dale AL, Tretli S, Kleinerman R, Sankila R, Hammarstrom L, Robsahm TE, Kaariainen H, Bregard A, Brondum-Nielsen K, Yuen J, Tucker M. Breast and other cancers in 1,445 blood relatives of 75 Nordic patients with ataxia telangiectasia. *Br J Cancer* 2005;93:260–265)**

Ionizing Radiation and Male Breast Cancer

Male breast cancers, diagnosed between 1958 and 1998, were identified among 45,880 male members of the Life Span Study cohort of Japanese atomic bomb survivors. Nine cases were diagnosed among exposed cohort members (crude rate = 1.8 per 100,000 person-years), three were diagnosed among non-exposed cohort members (crude rate = 0.5 per 100,000 person-years), and a dose-response relation was observed (excess relative risk per sievert = 8; CI = 0.8–48; $p = 0.01$). These findings add to the very limited information showing an association between radiation exposure and an increased male breast cancer risk. **(Ron E, Ikeda T, Preston DL, Tokuoka S. Male breast cancer incidence among atomic bomb survivors. *J Natl Cancer Inst* 2005;97:603–605)**

NIH AWARDS CEREMONY

Allan Hildesheim with Elias Zerhouni.

At the NIH Awards Ceremony held in July, **Allan Hildesheim, Ph.D.** (HREB) received the Director's Award in recognition of his leadership of the NCI Human Papillomavirus Vaccine (HPV) Trial 2005. In addition, **Linda Morris Brown, Dr.P.H.** (BB), received the Public Health Service Meritorious Service Award for her leadership and achievements in the area of cancer-related health disparities research. The awards were presented by NIH Director Dr. Elias A. Zerhouni.

Linda Morris Brown with Elias Zerhouni, David Elizalde, and Richard Wyatt.

Inflammatory Breast Carcinoma

Breast cancer cases diagnosed in the Surveillance, Epidemiology, and End Results (SEER) Program between 1988 and 2000 were classified as inflammatory breast carcinoma (IBC) ($n = 3{,}648$), non-inflammatory locally advanced breast cancer (LABC) ($n = 3{,}636$), or non-T4 breast cancer ($n = 172{,}940$). Between the 1988–1990 and 1997–1999 time intervals, IBC incidence rates (per 100,000 woman-years) increased from 2.0 to 2.5 ($p < 0.001$), whereas those for LABC declined (2.5 to 2.0; $p = 0.0025$), as did those for non-T4 breast cancer (108 to 101; $p = 0.0084$). IBC incidence rates were higher among black women (3.1) than among white women (2.2) ($p < 0.001$). Median survival of women with IBC (2.9 years) was shorter than that of women with LABC (6.4 years; $p < 0.0001$) or non-T4 breast cancer (> 10 years; $p < 0.0001$). Black women with IBC or LABC had poorer survival than white women ($p < 0.001$). Throughout the 1990s, IBC incidence rose, and survival improved modestly. Substantial racial differences were noted in age at diagnosis, age-specific incidence rates, and survival outcomes. **(Hance KW, Anderson WF, Devesa SS, Young HA, Levine PH. Trends in inflammatory breast carcinoma incidence and survival: The Surveillance, Epidemiology, and End Results Program at the National Cancer Institute. *J Natl Cancer Inst* 2005;97:966–975)**

CERVICAL CANCER

Risk in Women with Oncogenic HPV Types

The two-year absolute risk for cervical precancer attributable to infection by human papillomavirus type 16 (HPV-16) has not been definitively evaluated. Within the ALTS (Atypical Squamous Cells of Undetermined Significance/Low-Grade Squamous Intraepithelial Lesion Triage Study) population, baseline specimens of 5,060 women with equivocal or mildly abnormal cytology

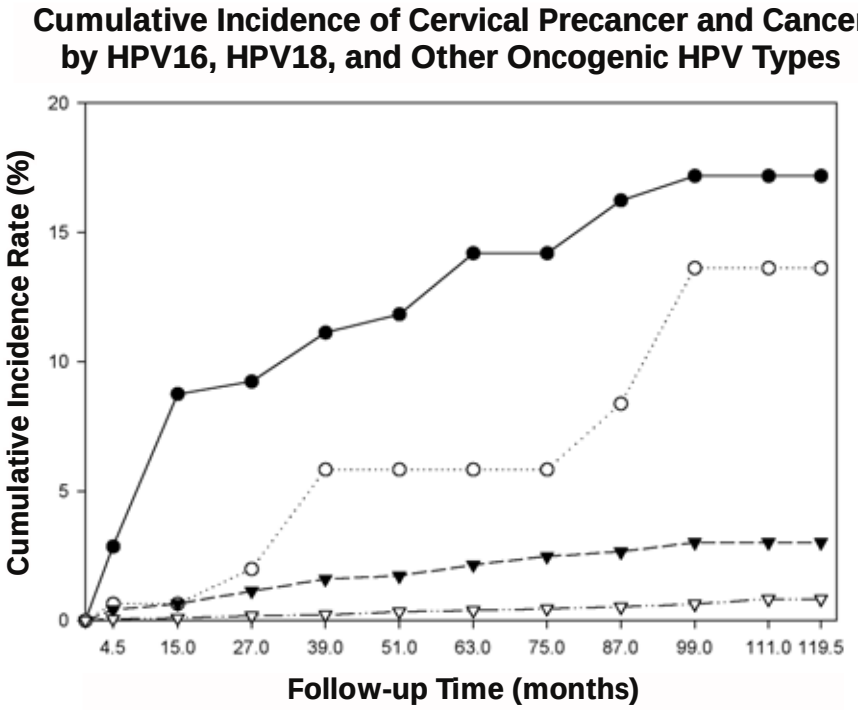


Figure 1. Cumulative incidence of cervical intraepithelial neoplasia grade 3 and cancer (≥ CIN3) over a 10-year period in 20,514 women according to oncogenic human papillomavirus (HPV) status at enrollment. HPV status is defined hierarchically as positive for HPV 16 (closed circles), positive for HPV18 (open circles), positive for the non-HPV16/18 oncogenic types in Hybrid Capture 2 (closed triangles), or oncogenic HPV negative (open triangles). (Khan MJ, et al. 2005)

were tested for HPV DNA. Absolute risks for diagnosis of cervical intraepithelial neoplasia Grade 3 (CIN3) or cancer during the two-year study period were calculated by status of HPV-16 and other oncogenic HPV types. A total of 542 women in the study group developed CIN3 or cervical cancer. Those who tested positive for HPV-16 had 38 times the risk for CIN3 or cervical cancer of women in the study who were HPV negative. Women who tested positive for other oncogenic HPV types had seven times the risk of women who tested HPV-negative. Thus, patients with a positive HPV-16 diagnosis may require more aggressive management than those who test positive for another oncogenic HPV type or who are HPV-negative. **(Castle PE, Solomon D, Schiffman M, Wheeler CM for the ALTS Group. Human papillomavirus type 16 infections and 2-year absolute risk of cervical precancer in women with equivocal or mild cytologic abnormalities. *J Natl Cancer Inst* 2005;97:1066–1071)**

In an analysis of 20,810 women enrolled in a cohort study based in the Kaiser Permanente health plan in Portland, Oregon, women who tested positive for HPV-16 or HPV-18 were diagnosed with CIN3 or cervical cancer more often than women who tested positive for another oncogenic HPV type or women who tested negative for HPV. Additional analysis of women with normal cytology at study enrollment provided further evidence for the observed risk differences. Screening for HPV-16 and HPV-18 separately from other oncogenic HPV types may identify women at greatest risk of developing CIN3 and cervical cancer, while allowing for less aggressive management of cases of other oncogenic HPV infections (see Figure 1). **(Khan MJ, Castle PE, Lorincz AT, Wacholder S, Sherman ME, Scott DR, Bush BB, Glass AG, Schiffman M. The elevated 10-year risk of cervical neoplasia in women with human papillomavirus (HPV) type 16 or 18 and the possible utility of type-specific HPV testing in clinical practice. *J Natl Cancer Inst* 2005;97:1072–1079)**

ESOPHAGEAL CANCER

Genome-wide Association Study

The authors report application of the Affymetrix, Inc. high-density single nucleotide polymorphism (SNP) array containing 11,555 SNPs in a pilot whole-genome association study of germline samples from 50 esophageal squamous cell carcinoma (ESCC) patients and 50 controls. Thirty-seven SNPs were associated with disease, assuming a recessive mode of transmission; similarly, 48 SNPs were identified assuming a dominant mode and 53 SNPs in a continuous mode. When the 37 SNPs identified from the generalized linear model (GLM) recessive mode were used in a principal components analysis, the first principal component correctly predicted 46 of 50 cases and 47 of 50 controls. Among all SNPs selected from GLMs for the three modes of transmission, 39 could be mapped to 1 of 33 genes. Many of these genes are involved in various cancers, including *GASC1*, shown previously to be amplified in ESCCs, and *EPHB1* and *PIK3C3*. Thus, the feasibility of the Affymetrix 10K SNP array in genome-wide association studies of common cancers is shown and new candidate loci for ESCC are identified. **(Hu N, Wang C, Hu Y, Yang HH, Giffen C, Tang ZZ, Han XY, Goldstein AM, Emmert-Buck MR, Buetow KH, Taylor PR, Lee MP. Genome-wide association study in esophageal cancer using GeneChip mapping 10K array. *Cancer Res* 2005; 65:2542–2546)**

LYMPHOMA

Alcohol Intake and Non-Hodgkin Lymphoma

Pooling original data from nine case-control studies from the United States, the United Kingdom, Sweden, and Italy in the International Lymphoma Epidemiology Consortium (InterLymph) yielded a study population of 6,492 non-Hodgkin lymphoma (NHL) cases and 8,683 controls. People who drank alcohol had a lower risk of NHL

than non-drinkers (OR = 0.83; CI = 0.76–0.89). Compared with non-drinkers, risk estimates were lower for current drinkers (OR = 0.73; CI = 0.64–0.84) than for former drinkers (OR = 0.95; CI = 0.80–1.14), but risk did not decrease with increasing consumption. The protective effect of alcohol did not vary by beverage type but did change with NHL subtype. The lowest risk estimates were recorded for Burkitt's lymphoma (OR = 0.51; CI = 0.33–0.77). Further study is needed to determine whether confounding lifestyle factors or immunomodulatory effects of alcohol explain this association. **(Morton LM, Zheng T, Holford TR, Holly EA, Chiu BC, Costantini AS, Stagnaro E, Willett EV, Dal Maso L, Serraino D, Chang ET, Cozen W, Davis S, Severson RK, Bernstein L, Mayne ST, Dee FR, Cerhan JR, Hartge P. Alcohol consumption and risk of non-Hodgkin lymphoma: A pooled analysis. *Lancet Oncol* 2005;6:469–476)**

Herbicides, Organochlorines, and Non-Hodgkin Lymphoma

To estimate the effects of residential pesticide exposure on risk of non-Hodgkin lymphoma (NHL), a population-based case-control study in Iowa and metropolitan Detroit, Los Angeles, and Seattle was conducted between 1998 and 2000. Computer-assisted personal interviews (1,321 cases, 1,057 controls) elicited data on pesticide use at each home occupied since 1970.

Herbicide use on the lawn or garden was similar among cases and controls (adjusted relative risk = 1.02; CI = 0.84–1.23). Estimated risk did not increase with greater duration, frequency, or total number of applications of herbicides to the lawn, garden, or to both combined. Risk was not elevated for respondents who applied the herbicides themselves or for those exposed during the 1970s, 1980s, or 1990s. The authors detected 2,4-dichlorophenoxyacetic acid equally often in dust taken from used vacuum cleaner bags in the current homes of cases and controls (78%) and dicamba in homes of 15% of cases and 20% of controls. They also found no elevation in risk among the respondents who had the highest dust levels and highest self-reported exposures. **(Hartge P, Colt JS, Severson RK, Cerhan JR, Cozen W, Camann D, Zahm SH, Davis S. Residential herbicide use and risk of non-Hodgkin lymphoma. *Cancer Epidemiol Biomarkers Prev* 2005;14:934–937)**

In another report from the same study, organochlorine concentrations were measured in vacuum cleaner bag dust from 603 white cases and 443 white controls who had owned most of their carpets for at least five years. NHL risk was elevated if any of the polychlorinated biphenyl (PCB) congeners (PCBs 105, 138, 153, 170, or 180) was detected (OR = 1.5; CI = 1.2–2.0). Risk was elevated in the top tertile of PCB 180 (OR = 1.7; CI = 1.1–2.6) and in the top two tertiles of total PCBs (middle tertile, OR = 1.6; CI = 1.1–2.4; top tertile, OR = 1.5; CI = 1.0–2.2). There was also a positive trend in risk with increasing PCB 180 levels (p for trend = 0.03). NHL risk was associated with detection of dichlorodiphenyldichloroethylene (DDE) (OR = 1.3; CI = 1.0–1.7) only among men, and a positive dose-response relationship was observed (p for trend = 0.02). **(Colt JS, Severson RK, Lubin J, Rothman N, Camann D, Davis S, Cerhan JR, Cozen W, Hartge P. Organochlorines in carpet dust and non-Hodgkin lymphoma. *Epidemiology* 2005;16:516–525)**

Hodgkin Lymphoma Susceptibility Gene

Hodgkin lymphoma (HL) has a strong familial component, but no genes have been identified. A genome-wide linkage screen was performed in 44 high-risk HL families with a total of 254 individuals providing DNA samples. Among these families, there were 95 HL cases and four cases of non-Hodgkin lymphoma (NHL) that were informative for linkage. Microsatellite markers (n = 1,058) were genotyped with an average spacing of 3.5 cM, and data were analyzed using both non-parametric and parametric linkage analysis, with both two-point and multipoint linkage statistics computed. The strongest linkage finding was on chromosome 4p near the marker D4S394. The lod score calculated by Genehunter Plus was 2.6 (nominal p = 0.0002) when both HL and NHL individuals were considered affected. The mean identity by descent sharing among 35 affected sibling pairs was 72% in this region (nominal p = 0.00007). The results are consistent with recessive inheritance. Other locations suggestive of linkage were found on chromosomes 2 and 11. The number of independent regions identified is more than expected by chance, although no one region met genome-wide significance levels. These linkage findings represent the first step towards identifying one or more loci leading to susceptibility to HL and understanding its complex etiology. **(Goldin LR, McMaster ML, Ter Minassian M, Saddlemire S, Harmsen B, Lalonde G, Tucker MA. A genome screen of families at high risk for Hodgkin lymphoma: Evidence for a susceptibility gene on chromosome 4. *J Med Genet* 2005;42:595–601)**

MALIGNANT MELANOMA

MC1R and *ASIP* Genes

Variants of the melanocortin-1 receptor (*MC1R*) gene and the Agouti signaling protein (*ASIP*) gene were examined among 267 melanoma patients and 382 control subjects from a case-control study and a family study in northeastern Italy in relation to phenotypic characteristics, sporadic and familial melanoma risk, and melanoma thickness. *MC1R* variant alleles were associated with a two- to fourfold increased risk of sporadic and familial melanoma compared with wild-type *MC1R*, particularly among individuals with multiple variant alleles (OR = 3.9; CI = 3.3–4.6). This association was stronger among individuals with fewer additional risk factors.

MC1R variant allele carriers were also three to four times more likely than non-carriers to have thick melanomas. The *ASIP* polymorphism was not associated with pigmentation, nevi, or melanoma risk. (Landi MT, Kanetsky PA, Tsang S, Gold B, Munroe D, Rebbeck T, Swoyer J, Ter Minassian M, Hedayati M, Grossman L, Goldstein AM, Calista D, Pfeiffer RM. MC1R, ASIP, and DNA repair in sporadic and familial melanoma in a Mediterranean population. *J Natl Cancer Inst* 2005;97:998–1007)

METHODS

Supplemented Case-control Design

The supplemented case-control design consists of a case-control sample and an additional sample of disease-free subjects who arise from a given stratum of one of the measured exposures in the case-control study. The supplemental data might, for example, arise from a population survey conducted independent of the case-control study. This design improves precision of estimates of main effects and especially of joint exposures, particularly when joint exposures are uncommon and the prevalence of one of the exposures is low. The authors first present a pseudo-likelihood estimator that is easy to compute. They further adapt two-phase design methods to find maximum likelihood estimates for the log odds ratios for this design and derive asymptotic variance estimators that appropriately account for the differences in sampling schemes of this design from that of the traditional two-phase design. (Pfeiffer RM, Chatterjee N. On a supplemented case-control design. *Biometrics* 2005;61:584–590)

SECOND CANCERS

Survivors of Childhood Soft Tissue Sarcoma

This study evaluated the risk of second cancers among 1,499 children (age < 18 years) who survived for at least one year after they were diagnosed with soft tissue sarcoma (STS) and who were reported to the SEER population-based cancer registries from 1973 to 2000. Twenty-seven children developed 28 subsequent primary malignancies, compared with 4.5 expected cancers based on general population rates (observed-to-expected ratio [O/E] = 6.3; CI = 4.2–9.1). The risk of developing a subsequent malignancy was increased among children with rhabdomyosarcoma (11 malignancies; O/E = 7.7), fibromatous neoplasms (9 malignancies; O/E = 5.8), and other STS (7 malignancies; O/E = 6.5). Initial therapy with radiation and chemotherapeutic agents was associated with a significantly higher risk compared with surgery alone (O/E = 15.2 vs.1.4; $p < 0.0001$). Elevated risks were observed for acute myeloid leukemia, cutaneous melanoma, female breast cancer, and sarcomas of the bone and soft tissue, with generally higher risks among patients who initially received combined modality therapy. For several children, the pattern of multiple malignancies was consistent with a genetic syndrome, particularly neurofibromatosis type 1 and Li-Fraumeni syndrome. (Cohen RJ, Curtis RE, Inskip PD, Fraumeni JF Jr. The risk of developing second cancers among survivors of childhood soft tissue sarcoma. *Cancer* 2005;103:2391–2396)

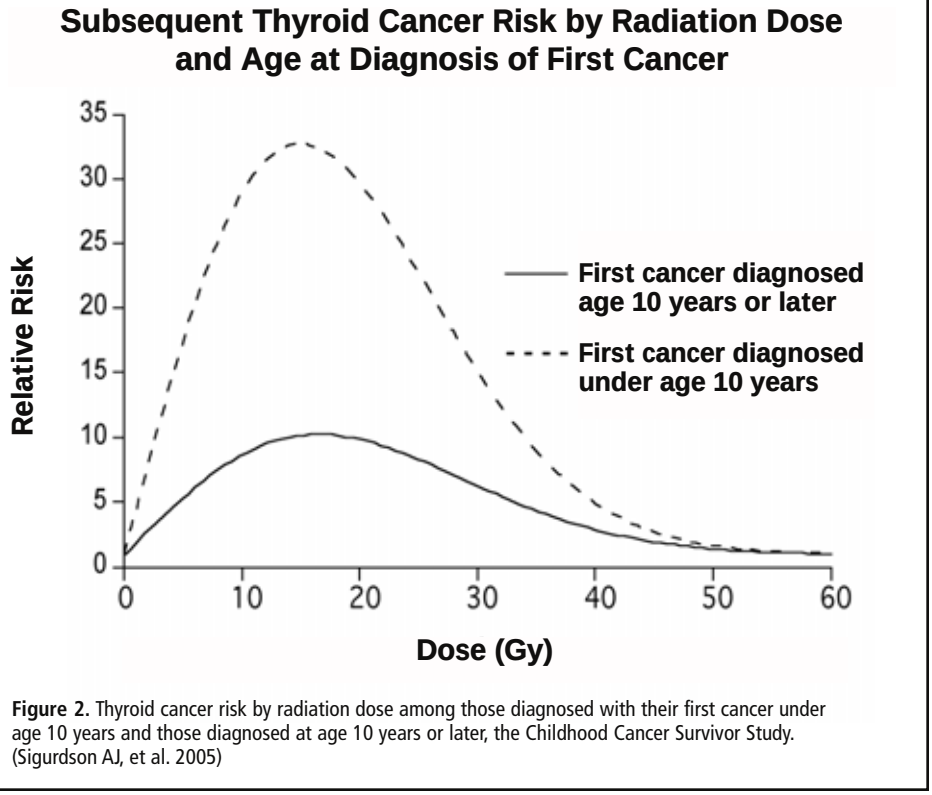


Figure 2. Thyroid cancer risk by radiation dose among those diagnosed with their first cancer under age 10 years and those diagnosed at age 10 years or later, the Childhood Cancer Survivor Study. (Sigurdson AJ, et al. 2005)

Thyroid Cancer after Childhood Cancer

This study aimed to quantify the long-term risk of thyroid cancer among survivors of malignant disease in childhood who had chemotherapy or radiotherapy to the head, neck, or upper thorax. In a nested case-control study, 69 cases with pathologically confirmed thyroid cancer and 265 controls were identified from 14,054 five-year survivors of cancer from the Childhood Cancer Survivor Study cohort. Risk of thyroid cancer increased with radiation doses up to 20–29 Gy (OR = 9.8; CI = 3.2–34.8). At doses greater than 30 Gy, a fall in the dose-response relation was seen, consistent with a cell-killing effect. Both the increased and decreased risks were more pronounced among those diagnosed with a first primary malignant disease before age 10 than among those older than 10 years (see Figure 2). The

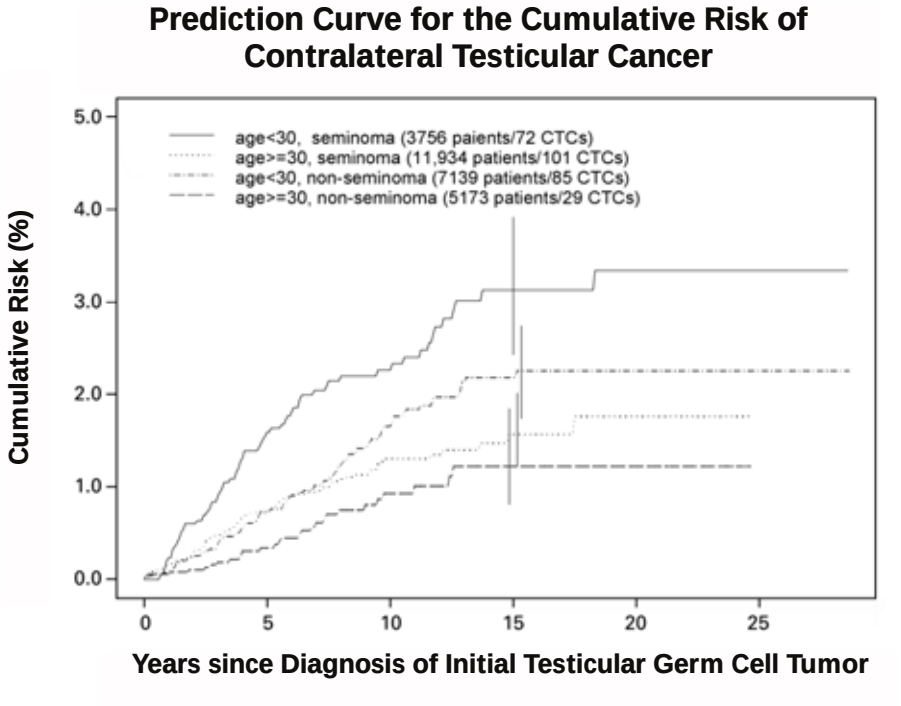


Figure 3. Cumulative risk of developing a metachronous contralateral testicular cancer in 28,002 patients with unilateral testicular germ cell tumor according to risk groups defined by age at initial diagnosis and initial histology. (Fossa SD, et al. 2005)

fall in risk remained when those diagnosed with Hodgkin lymphoma were excluded. Chemotherapy for the first cancer was not associated with thyroid-cancer risk, and it did not modify the effect of radiotherapy. **(Sigurdson AJ, Ronckers CM, Mertens AC, Stovall M, Smith SA, Liu Y, Berkow RL, Hammond S, Neglia JP, Meadows AT, Sklar CA, Robison LL, Inskip PD. Primary thyroid cancer after a first tumour in childhood (the Childhood Cancer Survivor Study): A nested case-control study. *Lancet* 2005;365:2014–2023)**

Squamous Cell Carcinomas after Graft-versus-Host Disease

Previous studies of recipients of hematopoietic stem-cell transplants suggest that graft-versus-host disease (GvHD) and its therapy may increase the risk for solid cancers, particularly squamous-cell carcinomas (SCCs) of the buccal cavity and skin. A case-control study of 183 patients with post-transplantation solid cancers (58 SCCs, 125 non-SCCs) and 501 matched control patients was conducted within a cohort of 24,011 patients who underwent hematopoietic stem-cell transplantation at 215 centers worldwide. Chronic GvHD and its therapy were strongly related to the risk for SCC, whereas no increase in risk was found for non-SCCs. Major risk factors for the development of SCC were long duration of chronic GvHD therapy, use of azathioprine, particularly when combined with cyclosporine and steroids, and severe chronic GvHD. The independent effects of immunosuppressive therapy and azathioprine could not be evaluated. Prolonged immunosuppressive therapy and azathioprine use were also significant risk factors for SCC of the skin and of the oral mucosa. Clinical screening for SCC is appropriate among patients exposed to persistent chronic GvHD, prolonged immunosuppressive therapy, or both. **(Curtis RE, Metayer C, Rizzo JD, Socie G, Sobocinski KA, Flowers ME, Travis WD, Travis LB, Horowitz MM, Deeg HJ. Impact of chronic GVHD therapy on the development of squamous-cell cancers after hematopoietic stem-cell transplantation: An international case-control study. *Blood* 2005;105:3802–3811)**

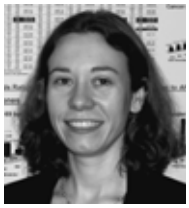
Risk of Contralateral Testicular Cancer

Although risk estimates for synchronous and metachronous contralateral testicular cancers vary widely, many clinicians recommend routine biopsy of the contralateral testis for patients with unilateral testicular cancer. Among 29,515 testicular cancer cases diagnosed before age 55 and reported to the NCI SEER Program from 1973 to 2001, 175 men presented with synchronous contralateral testicular cancer, and 287 men developed metachronous contralateral testicular cancer (O/E = 12.4; CI = 11.0–13.9). The 15-year cumulative risk was 1.9% (CI = 1.7%–2.1%). In multivariable analyses, non-seminomatous histology of the first testicular cancer was associated with a decreased risk of metachronous contralateral testicular cancer (hazard ratio [HR] = 0.60; CI = 0.46–0.79; $p < 0.001$) (see Figure 3). Increasing age at first testicular cancer diagnosis was associated with decreasing risk of non-seminomatous metachronous contralateral testicular cancer (OR = 0.90; CI = 0.86–0.94). The 10-year survival rate after metachronous contralateral cancer diagnosis was 93% (CI = 88%–96%), and that after synchronous contralateral cancer was 85% (CI = 78%–90%). The low cumulative risk of metachronous contralateral cancer and favorable overall survival of patients diagnosed with metachronous contralateral testicular cancer is consistent with the current U.S. approach of not performing a biopsy on the contralateral testis. **(Fossa SD, Chen J, Schonfeld SJ, McGlynn KA, McMaster ML, Gail MH, Travis LB. Risk of contralateral testicular cancer: A population-based study of 29,515 U.S. men. *J Natl Cancer Inst* 2005;97:1056–1066)**

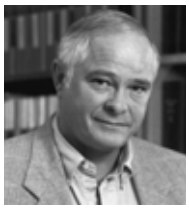
DCEG PEOPLE IN THE NEWS

Michael C. R. Alavanja, Dr.P.H., Occupational and Environmental Epidemiology Branch (OEEB), and **Matthew Bonner, Ph.D.** (OEEB), co-chaired an Agricultural Health Study Biomarker Workshop in March in Research Triangle Park, North Carolina. The proceedings were published in the *Journal of Biochemical and Molecular Toxicology* (Volume 19, Number 3, 2005).

Blanche Alter, M.D., M.P.H., Clinical Genetics Branch (CGB), gave a lecture on "Cancer-prone rare genetic syndromes: How do they instruct us?" at the Genome Damage and Stability Centre, University of Sussex in Brighton, England in June. Later in the month, Dr. Alter spoke on "MDS/AML in patients with Shwachman-Diamond Syndrome receiving long-term G-CSF" at the Third International Congress on Shwachman-Diamond Syndrome in Robinson College, Cambridge, England.


Gabriella Andreotti

Gabriella Andreotti, M.P.H., Hormonal and Reproductive Epidemiology Branch (HREB), had an abstract entitled "Polymorphism of genes in the lipid metabolism pathway and the risk of biliary tract cancers: A population-based study in Shanghai, China" accepted for the Second Annual NIH Graduate Student Research Symposium, which was held in April.


Robert Biggar

Robert Biggar, M.D., Viral Epidemiology Branch (VEB), gave a presentation on "Mother-child HLA concordance as a risk factor for HTLV-I transmission" at the 12th International Conference on Human Retrovirology: HTLV and Related Viruses in Montego Bay, Jamaica in June.


New FELCOM Representatives: Shih-Chen Chang and Hong Hong Zhu.

Shih-Chen Chang, Ph.D., Nutritional Epidemiology Branch (NEB), and **Hong Hong Zhu, M.D., M.H.S., M.Sc.** (OEEB), have been appointed to represent DCEG on the NIH Fellows Committee, also known as FELCOM. They are replacing **Beth Brown, Ph.D.** (VEB), and **Mathew Bonner, Ph.D.** (OEEB).


Aaron Blair

Aaron Blair, Ph.D. (OEEB), gave an invited talk on "The interaction of science and ethics on issues in occupational health" at the International Conference in Memory of Olav Axelson in Borgholm, Sweden in May. Later in June, Dr. Blair and **Michael Hauptmann, Ph.D.,** Biostatistics Branch (BB), organized a meeting of a working group at the NCI in Rockville to discuss updating their study of a cohort of industrial workers exposed to formaldehyde. The working group consisted of Dr. Elisabeth Fontham (Louisiana State University), Dr. Michael Thun (American Cancer Society), and Dr. Noah Seixas (University of Washington); the meeting was attended by representatives from industry, unions, the U.S. Environmental Protection Agency (EPA), and advocacy groups.


Philip Castle

Philip Castle, Ph.D. (HREB), spoke on "Natural history of HPV infection and the role of the cervical microenvironment" at Brigham and Women's Hospital, Harvard University in May. He then gave talks on "New strategies for cervical cancer prevention" for the Community Networks Cancer Health Disparities Summit 2005 in Rockville, Maryland in July, and on "HPV DNA testing in cervical cancer screening" at the Centers for Disease Control and Prevention in Atlanta in August. Dr. Castle also chaired a panel discussion on "Clinical utility of genomic HPV testing" at the 22nd International Papillomavirus Conference in Vancouver, British Columbia, Canada in May.

Nilanjan Chatterjee, Ph.D. (BB), addressed a symposium in applied and computational mathematics at the New Jersey Institute of Technology in Newark in May. The title of his talk was "Semiparametric maximum-likelihood estimation exploiting gene-environment independence in case-control studies." He also gave a talk entitled "Exploiting gene-environment independence in family-based case-control studies: Increased power for detecting associations, interactions, and joint effects" at the International Chinese Statistical Association's Applied Statistical Symposium in Bethesda, Maryland in June.

Mustafa Dosemeci, Ph.D. (OEEB), and **Patricia Stewart, Ph.D.** (OEEB), spoke on "Exposure estimation in occupational epidemiology studies" at a National Academies of Sciences meeting held in Irvine, California in June.

Mary Lou McMaster

Mary Lou McMaster, M.D. (GEB), received the Surgeon General's Exemplary Service Award for her work as director of the Public Health Service Choral Ensemble for the past four years.

Eric Engels, M.D., M.P.H. (VEB), gave an invited talk on "Chronic immune stimulation and non-Hodgkin lymphoma" at the University of Southern California in Los Angeles in April. He also gave a talk on "Lung cancer in people with HIV infection" at the University of Texas M.D. Anderson Cancer Center in Houston in June.

Mitchell Gail

Mitchell Gail, M.D., Ph.D. (Chief of BB), spoke on the topic "On criteria for evaluating models of absolute risk" at the University of Rochester in April. He also gave an invited talk entitled "Using case-control and case-only probands with family history to estimate genotype-specific cumulative risk" at the American Statistical Association meeting in Minneapolis in August.

Ethel Gilbert

Ethel Gilbert, Ph.D., Radiation Epidemiology Branch (REB), gave two invited talks: "Recent epidemiologic data contributing to cancer risk assessment" at the annual Society of Nuclear Medicine meeting in Toronto in June and "The Biological Effects of Ionizing Radiation (BEIR VII) report's models for estimating cancer risks" at the annual Health Physics Society meeting in Spokane, Washington in July.

James Goedert, M.D. (Chief of VEB), gave a lecture entitled "Breast cancer: Is there a human virus?" at the University of Palermo in Italy in July.

Mark Greene, M.D. (Chief of CGB), gave a talk on "New cancer genes and syndromes" at a conference on Cancer Control through Genetics at the University of Chicago Center for Clinical Cancer Genetics in June.

Patricia Hartge, Sc.D., Epidemiology and Biostatistics Program (EBP), chaired the Family History session and spoke on "Summary of progress and future direction" at the annual International Lymphoma Epidemiology Consortium (InterLymph) meeting in York, England in July.

Marianne Henderson, M.S., Chief of the Office of Division Operations and Analysis (ODOA), co-led a workshop on "Designing and developing a repository database" at the annual International Society for Biological and Environmental Repositories meeting in Seattle in May. Her presentation focused on the data management considerations and challenges faced by large biorepositories.

Michie Hisada

Michie Hisada, M.D., Sc.D. (VEB), chaired the Epidemiology Workshop at the 12th International Conference on Retrovirology: HTLV and Related Viruses in Montego Bay, Jamaica in June.

Ann Hsing, Ph.D. (HREB), gave a presentation on "Reproducibility data on GC-MS and RIA serum and tissue assays" at the Endogenous Hormones and Prostate Cancer Collaborative Group meeting held at Oriel College in Oxford, England in June. She also gave a talk on the epidemiology of prostate and biliary tract cancers at the Cancer Research United Kingdom Epidemiology Unit, University of Oxford. In addition, Dr. Hsing became a member of the Editorial Board of *Cancer Epidemiology, Biomarkers & Prevention* in August.

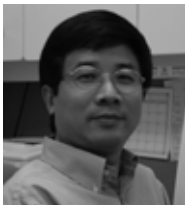

Jose Jeronimo

Jose Jeronimo, M.D. (HREB), gave a talk on "Colposcopic evaluation of HPV positive patients" at the 12th World Congress of Cervical Pathology and Colposcopy, organized by the International Federation of Cervical Pathology and Colposcopy, in Cancun, Mexico in June. He spoke on "A new approach to HPV testing and cervical cancer screening" at the July NCI Community Networks Cancer Health Disparities Summit.

Daehee Kang, M.D., Ph.D. (OEEB), gave an invited talk on "The gene-environment interactions of breast cancer" at the Columbia University School of Public Health in June.

Ruth Kleinerman, M.P.H. (REB), presented a talk on "Risk of new cancers following radiotherapy in long-term survivors of retinoblastoma" at the International Society of Genetic Eye Diseases and International Retinoblastoma Symposium in Whistler, British Columbia, Canada in September.

Ola Landgren, M.D., Ph.D., Genetic Epidemiology Branch (GEB), gave a talk entitled "Outcome is improving in chronic lymphocytic leukemia: A population-based study on 9,756 patients diagnosed in Sweden 1973–2001" at the 10th Congress of the European Hematology Association in Stockholm in June.


Hong-Chuan Li

Hong-Chuan Li, Ph.D. (VEB), gave a presentation on "Serologic and molecular characteristics of atypical HTLV Western blot banding patterns in Jamaican blood donors" at the 12th International Conference on Human Retrovirology: HTLV and Related Viruses in Montego Bay, Jamaica in June.

Martha Linet, M.D., M.P.H. (Chief of REB), presented a talk on "Radiation spectrums and mechanisms: An overview of the role of radiation in the etiology of childhood leukemia" at the Childhood Leukemia Workshop at the Institute of Child Health in London in April. She also gave a talk on "Epidemiological and dosimetry needs after radiation disasters: Lessons from six decades of studies" to the Radiation Nuclear Federal Interagency Working Group at the National Institute of Allergy and Infectious Diseases in Bethesda, Maryland in May.


Lee Moore

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

Lindsay Morton, Ph.D. (HREB), spoke on "Proposed nested classification of lymphoma subtypes for use in epidemiologic studies" at the July InterLymph meeting in York, England.

Jay Nuckols, Ph.D. (OEEB), organized and chaired a session on "Exposure considerations for emerging chemical by-products due to alternative water disinfection practices" at the EPA's Optimizing the Design and Interpretation of Epidemiologic Studies to Consider Alternative Disinfectants of Drinking Water Workshop in Raleigh, North Carolina in June.

June Peters, M.S., C.G.C. (CGB), served on the Scientific Advisory Committee and as an abstract reviewer, session moderator, and presenter at the Ninth International Psychosocial Aspects of Hereditary Cancer meeting in Philadelphia in June. She also spoke on "Family systems and genetic counseling" for the clinical supervisors of the Genetic Counseling Training Program at Sarah Lawrence College in Bronxville, New York in July.

Charles Rabkin, M.D. (VEB), gave invited talks on "Molecular epidemiology of AIDS-related lymphoma" at Alfried Krupp College and at the Ernst Moritz Arndt University in Greifswald, Germany in July.

Elaine Ron, Ph.D. (REB), gave talks on "Thyroid cancer patterns in countries belonging to the Middle East Cancer Consortium (MECC)" and "Brain and other CNS cancer patterns in countries belonging to the MECC" in Lyon, France in June. Later that month, she also spoke about the U.S. Radiologic Technologists Health Study at the Health Protection Agency in Chilton, England.

Arthur Schatzkin, M.D., Dr.P.H. (Chief of NEB), delivered a lecture entitled "Promises and perils of validating biomarkers for cancer risk" at a Joint U.S. Food and Drug Administration (FDA)–NCI–Office of Dietary Supplements Workshop on Use and Misuse of Biomarkers as Indicators of Cancer Risk Reduction Following Dietary Manipulation in Bethesda, Maryland in July.

Rashmi Sinha, Ph.D. (Deputy Chief of NEB), gave a talk on "Meat-derived carcinogens and cancer" at the FDA National Center for Toxicological Research in Jefferson, Arkansas in May. In September, Dr. Sinha and **Michael Leitzmann, M.D., Dr.P.H.** (NEB), presented talks on "Diet and cancer epidemiologic studies in developing countries" and "Dietary measurement error: What next?" as well as "Assessment and validation of physical activity in epidemiologic studies"

and "Physical activity in epidemiologic studies," respectively, at the Asia Cohort Consortium meeting in Seoul, South Korea. A few days later, Dr. Sinha also gave a talk on "The options in dietary assessment method for large cohort studies" at the School of Public Health at Seoul National University.


Philip Taylor

Philip Taylor, M.D., Sc.D. (GEB), spoke on "Genome-wide association study in esophageal cancer using GeneChip 10K array" at the Digestive Diseases Week in Chicago in May. In addition, Dr. Taylor gave a talk on "Genetics in the etiology, early detection, and prevention of upper gastrointestinal cancers" at the Cancer Institute, Chinese Academy of Medical Sciences in Beijing in June.

Lois B. Travis, M.D., Sc.D. (REB), chaired a session on "Cancer survivorship: Long-term effects of treatment" at the annual American Society of Clinical Oncology (ASCO) meeting in June. She has also been appointed to the National ASCO Cancer Survivorship Task Force.

Margaret A. Tucker, M.D. (Chief of GEB), gave talks on "Prevention and detection of early stage melanoma," "Dissecting risk modifiers in inherited cancer syndromes," and "Melanoma genetics: Where are we?" at the ASCO meeting in Orlando in May. She also chaired an educational session entitled "Update on inherited cancer syndromes: Beyond breast, ovarian, and colon cancers" at the same meeting.

Sholom Wacholder, Ph.D. (BB), participated in an invited session on "Bayesian methods in cancer research" at the American Statistical Association meeting in Minneapolis in May. He gave another invited lecture, "What is the chance of an incorrect conclusion about a test of association between a genetic variant and risk of cancer?" at a Memorial Symposium for Baruch Modan at Chaim Sheba Hospital in Tel Hashomer, Israel in the same month. He also addressed the Annual Israeli Statistical Association meeting in Tel Aviv on "What is the chance that a negative report is a false negative?"

Sophia Wang, Ph.D. (HREB), spoke on "The role for identifying common genetic polymorphisms in cancers with unknown and known etiologies: Non-Hodgkin lymphoma and cervical neoplasia" at the University of British Columbia and British Columbia Cancer Research Centre in Vancouver, Canada in May. Also in that month, Dr. Wang was an invited speaker on "Methylation events in cervical cancer: Identification in tissue and validation in cytology specimens" at the Johns Hopkins School of Medicine. In addition, she gave a talk on "Family history of hematopoietic malignancies and risk for non-Hodgkin lymphoma" at the InterLymph meeting in York, England in July.

Elyse Wiszneauckas, a Scientific Program Specialist (ODOA), received a B.S. degree in Information Systems Management from the University of Maryland University College in August.

Hong Hong Zhu, M.D. (OEEB), gave a presentation on "Secondhand tobacco smoke and breast cancer: A nested case-control study in the Shanghai Women's Health Study" at the CCR Combined Faculty Retreat in Cumberland, Maryland in July, which was sponsored by the Breast and Gynecologic Malignancies Faculty, the Cancer Prevention Faculty, and the Mouse Models for Mammary Cancer Collective.

Several DCEG researchers recently received funding support from the NIH Office of Rare Diseases. **Aaron Blair, Ph.D.** (OEEB), will develop an International Consortium for Studies of Cancer and Other Diseases in Agricultural Populations. **Allan Hildesheim, Ph.D.** (HREB), **Ann Hsing, Ph.D.** (HREB), and **Charles Rabkin, Ph.D.** (VEB), will hold a workshop on Chronic Inflammation and Cancer: Biology, Pathology, Immunology, and Epidemiology. **Elaine Ron, Ph.D.** (REB), will conduct a research project on the ALARA Concept in Pediatric Interventional and Fluoroscopic Imaging.


Rashmi Sinha

Rashmi Sinha, Ph.D. has recently been appointed Deputy Branch Chief of the Nutritional Epidemiology Branch (NEB). In this new position, her responsibilities include developing a program for career development for junior investigators within the Branch. In particular, she will coordinate the recruitment, training, and professional development of tenure-track investigators and pre- and post-doctoral fellows. Dr. Sinha will also promote collaborative activities within ongoing Division studies.

COMINGS . . . GOINGS


Mohamad Al-Rahawan

Mohamad Al-Rahawan, M.D., a pediatric hematology/oncology fellow at Children's National Medical Center and George Washington University Medical Center in Washington, D.C., has joined the Clinical Genetics Branch (CGB) as a special volunteer. He will be performing the research component of his training program. Dr. Al-Rahawan began his pediatric hematology/oncology training at the University of Virginia in Charlottesville before moving to Washington, DC. He will be working with **Blanche Alter, M.D., M.P.H.,** and **Neelam Giri, M.D.,** on the Inherited Bone Marrow Failure Syndromes protocol.


William Anderson

William Anderson, M.D., M.P.H., has joined the Biostatistics Branch (BB) as a tenure-track investigator. Dr. Anderson is board-certified in internal medicine, hematology, and medical oncology. He earned an M.P.H. in epidemiology before joining the Division of Cancer Prevention (DCP) in 2000. In DCP, he began a series of studies into the descriptive epidemiology of cancer, some in collaboration with staff members from DCEG. Dr. Anderson will develop a research program on descriptive epidemiology, focusing on its connections to clinical findings and analytical epidemiology, particularly for breast cancer.


Stefan Boehringer

Stefan Boehringer, M.D., has joined BB as a special volunteer and will be working on gene association studies with **Ruth Pfeiffer, Ph.D.** He received a degree in medicine from the University of Bochum, Germany, with further training and experience at Essen University, where he worked in the Department of Human Genetics. He is currently completing a Ph.D. dissertation in statistics at the University of Dortmund.

Matthew Bonner, Ph.D., a postdoctoral fellow in the Occupational and Environmental Epidemiology Branch (OEEB) since 2003, has accepted a faculty position at the State University of New York at Buffalo. While at DCEG, he worked on the Agricultural Health Study, investigating associations between pesticide exposures and cancer. He also worked on the role of radon exposure, exposure to smoky coal, and genetic polymorphisms in the etiology of lung cancer.


Gabriel Chodick

Gabriel Chodick, Ph.D., has joined the Radiation Epidemiology Branch (REB) as a postdoctoral fellow. Dr. Chodick was an epidemiologist in Maccabi Health Care Services, the second largest health maintenance organization in Israel. He received a Ph.D. in epidemiology and preventive medicine from the Tel Aviv University Medical School in 2003. Dr. Chodick will work on an extended follow-up of a cohort of more than 35,000 hyperthyroid patients treated with radioiodine, surgery, or drugs.

Ben Hulley, a predoctoral CRTA fellow in the Genetic Epidemiology Branch (GEB), was recently accepted into the School of Medicine at the University of California, San Diego. During his time in GEB, he worked with **Mary Lou McMaster, M.D.,** on long-term outcomes associated with familial Waldenström's macroglobulinemia. He also worked with **Maria Teresa Landi, M.D., Ph.D.,** on the role of genes involved in regulation of the immune system and of pigmentation in the development and progression of malignant melanoma.

Michelle Khan, M.P.H., recently finished a two-year program as a Howard Hughes Medical Institute (HHMI)-NIH Research Scholar, working with **Mark Schiffman, M.D., M.P.H.** (HREB), and returned to the University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School as a third

Robert N. Hoover, Sc.D., M.D., Epidemiology and Biostatistics Program (EBP), was awarded the 22nd Abraham Lilienfeld Award for lifetime contributions to epidemiology. His career is marked by 30 years at the NCI. He has held positions of ever increasing responsibility within the research infrastructure, from staff associate to Director of EBP, and his resume contains nearly 400 publications. This outstanding career was recognized by the American College of Epidemiology in September.


Robert N. Hoover

year medical student. While with HREB, she authored seven papers, including two in the *Journal of the National Cancer Institute.* In recognition of her remarkable progress at NIH, Ms. Khan won a Continuing Support for Completion of Medical Studies Research Training fellowship from HHMI, a fully funded award for the current year in medical school.


Sheng Luo

Sheng Luo, Ph.D., joined BB in August as a visiting fellow. Dr. Luo has master's degrees in statistics and engineering and a Ph.D. in applied mathematics. He is now a Ph.D. candidate in biostatistics at Johns Hopkins Bloomberg School of Public Health. Dr. Luo will be working on his dissertation project with **Nilanjan Chatterjee, Ph.D.**


Rajeev Mahajan

Rajeev Mahajan, M.S., has joined OEEB as a predoctoral fellow. He received an M.S. in epidemiology from Johns Hopkins Bloomberg School of Public Health. Mr. Mahajan will investigate associations between pesticide exposures and cancers. He will also be developing a biomarker protocol to investigate the carcinogenic mechanisms of certain pesticides.


Alyssa Voss Minutillo

Alyssa Voss Minutillo, M.P.H., has returned to the DCEG Office of the Director as a technical writer/editor. Ms. Minutillo, who has an undergraduate degree in biology from Simmons College, first joined the Division as a health communications fellow in 2002 while completing her M.P.H. degree from the University of South Florida. Upon finishing her NCI fellowship, she worked as a Research Associate at the George Washington University Biostatistics Center, coordinating multicenter clinical trials for the National Institute of Diabetes and Digestive and Kidney Diseases on the prevention and treatment of pediatric type 2 diabetes.

Beata Peplonska, M.D., Ph.D., has returned to the Nofer Institute of Occupational Medicine in Lodz, Poland after spending a year sabbatical in OEEB. She was a field manager for the Lodz component of the collaborative Breast Cancer Study in Poland. During her year in DCEG, she analyzed data on occupational exposures and physical activity in the development of breast cancer.

Tanuja Rastogi, Sc.D., a postdoctoral fellow in the Nutritional Epidemiology Branch (NEB), became a science policy fellow with the U.S. State Department in Washington, D.C., in September as part of an American Association for the Advancement of Science fellowship program. Dr. Rastogi joined NEB in 2002 and worked on a pilot study for a cohort in India as well as study of cancer incidence rates among Asian Indians residing in several countries, including the United States.


Melissa Rotunno

Melissa Rotunno, Ph.D., has joined GEB as a postdoctoral fellow. She has a B.S. and a Ph.D. in physics from the University of Milan. Dr. Rotunno will be working with **Maria Teresa Landi, M.D., Ph.D.,** and **Neil Caporaso, M.D.,** on the analyses of complex genomic and epidemiologic data from a case-control study of lung cancer.

Sheri Dixon Schully, Ph.D., a Presidential Management Fellow, has joined the Office of Division Operations and Analysis (ODOA) for a three-month internship. Dr. Schully received a Ph.D. in biological sciences from Louisiana State University in 2005. Her doctoral work focused on evolutionary genetics using Drosophila as a model system. She will be developing a communication plan for the Cancer Genetics Markers of Susceptibility (CGEMS) project with **Marianne Henderson, M.S.**


Sheri Dixon Schully


Shunro Sonoda

Shunro Sonoda, M.D., Ph.D., has joined the Viral Epidemiology Branch (VEB) as a visiting scientist. His expertise is in virology and immunology, with particular emphasis on human T-lymphotropic virus type I (HTLV-I) and the human leukocyte antigen system. At the Kagoshima University Faculty of Medicine in Japan, he was professor and chair of the Department of Virology from 1990 to 2001 and professor and chair of the Department of Island Medicine from 2001 to 2003. At VEB, Dr. Sonoda will help with studies of HTLV-I infection and the related diseases, adult T-cell leukemia and HTLV-1-associated myelopathy/tropical spastic paraparesis, in Jamaica, where HTLV-1 is endemic.

Isabelle Thierry-Chef, Ph.D., a visiting fellow in REB, is joining the International Agency for Research on Cancer, where she will be studying the effects of plutonium on the risk of lung cancer. During her year at REB, Dr. Thierry-Chef assessed doses of ionizing radiation due to medical exposures in a study of pediatric patients undergoing interventional radiology procedures and a study of breast doses from different types of diagnostic examination.

Anne C.M. Thiébaut, Ph.D., has joined NEB as a visiting fellow. She received her


Anne C.M. Thiébaut

doctoral degree at the National School of Statistics and Information Analysis in France and an M.P.H. in epidemiology at the University of Paris XI. She will evaluate the association between breast cancer risk and dietary fatty acid intake in the American Association of Retired Persons (AARP) cohort study. She also plans to investigate the impact of measurement error on dietary associations with cancer.


Jocelyn Weiss

Jocelyn Weiss, Ph.D., has joined OEEB as a postdoctoral fellow. She has a B.S. in biology and child development and an M.P.H. in epidemiology and biostatistics, both from Tufts University. She recently obtained a Ph.D. in epidemiology from the University of Washington in Seattle. For her dissertation, she studied polymorphisms in nucleotide excision repair genes and risk of endometrial cancer. Dr. Weiss will be working with **Richard Hayes, D.D.S., Ph.D.,** on the investigations of cancer risk in the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial.

Kelly Yu, M.P.H., has joined HREB as a predoctoral fellow. She is currently a student in the Department of Epidemiology at Johns Hopkins Bloomberg School of Public Health. Ms. Yu received an M.P.H. in chronic disease epidemiology from Yale University in 2000. She will be working on a follow-up study of high-risk individuals from a cohort of multiplex families with nasopharyngeal cancer in Taiwan with **Allan Hildesheim, Ph.D.**

Mingdong Zhang, M.D., Ph.D., a research fellow in VEB, has accepted a position as an assistant professor at the Center for Emerging Infectious Disease, Chinese University of Hong Kong.

Yawei Zhang, M.D., Ph.D., an HREB postdoctoral fellow, recently began work as an assistant professor in the Department of Epidemiology and Public Health at the Yale University School of Medicine. While with HREB, she focused on early-life exposure to maternal hormones in relation to testicular cancer risk, on DNA repair genes in relation to breast cancer risk, and on genetic susceptibility to non-Hodgkin lymphoma.

DCEG PARTICIPATES IN SOCIETY FOR EPIDEMIOLOGIC RESEARCH MEETING

DCEG researchers participated in the Joint Meeting of the Society for Epidemiologic Research (SER) and the Canadian Society for Epidemiology and Biostatistics in Toronto in June by presenting posters and moderating educational sessions on their work. As president of SER, **Maureen Hatch, Ph.D.,** Radiation Epidemiology Branch (REB), delivered the presidential address on "Epidemiology without borders," which was the theme of the meeting. She called for epidemiologists to extend their professional activities beyond national or disciplinary borders, not only to achieve an important scientific or public health result, but also to stimulate new ideas and develop new partnerships. "The present and future of epidemiology lie in transdisciplinary team science," she said. "The new challenge is partnership with quite different disciplines."

The annual three-day event also featured a keynote address by Dr. George Davey-Smith, University of Bristol, and workshops, symposia, roundtables, poster sessions, and special exhibits by various epidemiologic programs.

In addition to Dr. Hatch, other DCEG staff also played leadership roles in the meeting. **Louise Brinton, Ph.D.** (HREB), gave a presentation at a spotlight session and also led a roundtable on "Unresolved issues regarding exogenous hormones and cancer risk." **Patricia Hartge, Sc.D.** (EBP), presented a poster on "Reporting participation in epidemiologic studies: A survey of practice" and ran a symposium entitled "The changing face of epidemiology" with Dr. David Hunter, Harvard University, and Dr. John Potter, Fred Hutchinson Cancer Research Center, at which she also spoke.

Rachael Stolzenberg-Solomon, Ph.D. (NEB), delivered a talk which was also selected for oral presentation in a spotlight session on cancer called "Pathways to cancer: Lifestyle, obesity, and metabolism." **Sholom Wacholder, Ph.D.** (BB), organized a symposium entitled "When should a finding be considered positive? Alternatives to p-value < 0.05, 95% confidence intervals, and Bonferroni correction," at which he also spoke.

DCEG PRESENTERS

Kenneth Adams, Ph.D. (NEB): Association between body mass and colon cancer

Matthew Bonner, Ph.D. (OEEB): Malathion exposure and cancer incidence in the Agricultural Health Study

Louise Brinton, Ph.D. (HREB): Relationship of benign gynecologic diseases to subsequent risk of ovarian and uterine cancers

Jinbo Chen, Ph.D. (BB): Quantifying selection bias in epidemiologic studies

Patricia Hartge, Sc.D. (EBP): Declining participation: How bad is it? What is the solution?

Unhee Lim, Ph.D. (NEB): Anthropometric indicators and risk of lymphoid malignancies in the prospective NIH-AARP diet and health study

Katherine McGlynn, Ph.D. (HREB): Relationship between cryptorchism and maternal hormone levels

Mark Purdue, Ph.D. (OEEB): Hormone replacement therapy and colorectal adenomas: Data from the PLCO Cancer Screening Trial

Cecile Ronckers, Ph.D. (REB): Radiation and thyroid cancer in the Childhood Cancer Survivor study: A detailed evaluation of dose-response and its modifiers

Rachael Stolzenberg-Solomon, Ph.D. (NEB): Insulin, glucose, insulin resistance, and pancreatic cancer in male smokers

Margaret Wright, Ph.D. (NEB): Serum vitamin E in relation to total and cause-specific mortality in the Alpha-tocopherol, Beta-carotene study

Sholom Wacholder, Ph.D. (BB): When should a finding be considered positive? Alternatives to p-value < 0.05, 95% confidence intervals, and Bonferroni correction

VISITING SCHOLAR MICHAEL THUN

Dr. Michael Thun, Vice President of Epidemiology and Surveillance Research at the American Cancer Society (ACS), spent two days in May at DCEG as a Visiting Scholar. Dr. Thun, who leads the ACS Cancer Prevention Study-II Nutrition Cohort, has had a distinguished career in cancer epidemiology and public health focused on the role of tobacco, pharmaceutical agents, nutrition, occupational exposures, and genetic susceptibility in the causation of human cancer. Dr. Thun was one of the first investigators to demonstrate a reduced risk of colon cancer among regular aspirin users, thereby prompting a surge of interest in the relation between inflammation and carcinogenesis. His work on tobacco has included contributions to consensus reports of the U.S. Surgeon General and the International Agency for Research on Cancer. He currently holds adjunct professorships at the Rollins School of Public Health and Winship Cancer Institute of Emory University.

In his keynote address, Dr. Thun presented a thought-provoking seminar entitled "Absolute risks: What does the orphan of epidemiology have to teach us?" in which he outlined the relevance of absolute risk estimates to average and individual risks (e.g., Gail and Harvard risk models). He also discussed risk-benefit evaluations, the development and delivery decision-making process, and epidemiologic applications. Expanding on this topic, he related absolute individual risk estimates to absolute population burden, using attributable mortality from obesity as a case study (see Figure 1). Dr. Thun highlighted the wide range in estimated U.S. deaths attributable to obesity in recent publications and related it to choice of referent group (and the problem of reverse causation), uncontrolled confounding, small population size with limited statistical power, and some random error. In conclusion, Dr. Thun emphasized that accurate relative risk estimates are vital to the development of reliable population attributable risk estimates.

Following the talk, **Joseph F. Fraumeni, Jr., M.D.,** DCEG Director, presented Dr. Thun with a plaque in recognition of his distinguished contributions to cancer epidemiology and his service as a member of the NCI Board of Scientific Counselors.

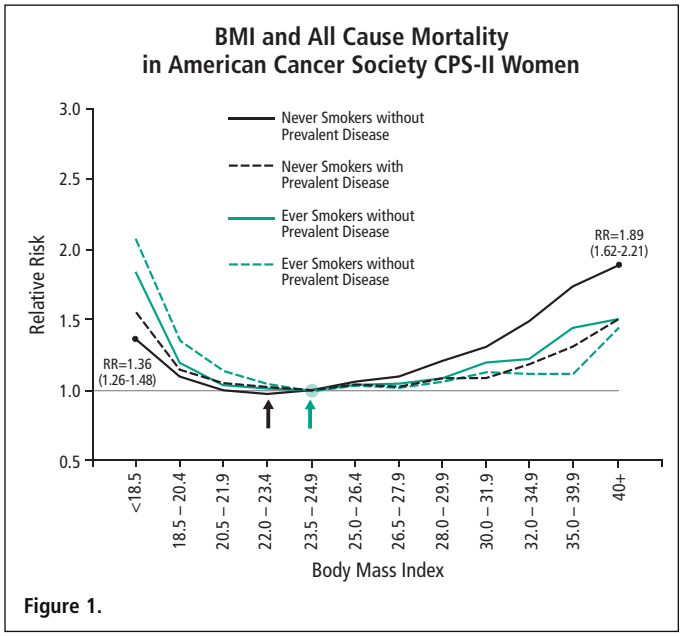


Figure 1.

Over the course of the two-day visit, Dr. Thun met with various groups and held a lunch-time discussion of career issues with DCEG fellows. In a series of meetings, he provided advice on current DCEG research efforts, including sessions on tobacco, molecular epidemiology, and lung cancer led by **Neil Caporaso, M.D.** (Genetic Epidemiology Branch [GEB]), **Maria Teresa Landi, M.D., Ph.D.** (GEB), and **Andrew Bergen, Ph.D.** (GEB); the role of inflammation and NSAIDs led by **Sophia Wang, Ph.D.** (Hormonal and Reproductive Epidemiology Branch [HREB]), and **Eric Engels, M.D., M.P.H.** (Viral Epidemiology Branch); and a variety of other topics, including the NCI Cancer Genetic Markers of Susceptibility (CGEMS) project with Dr. Fraumeni, **Stephen Chanock, M.D.** (Core Genotyping Facility), and **Robert Hoover, M.D., Sc.D.** (Epidemiology and Biostatistics Program), and the ongoing NCI-ACS collaborative study involving **Ann Hsing, Ph.D.** (HREB). The visit culminated with a timely session dedicated to obesity and cancer led by **Michael Leitzmann, M.D., Dr.P.H.** (Nutritional Epidemiology Branch [NEB]), and **Arthur Schatzkin, M.D., Dr.P.H.** (NEB), followed by a review of the NCI Energy Balance Initiative by Dr. Rachel Ballard-Barbash of NCI's DCCPS and a presentation by **Barry Graubard, Ph.D.,** of the Biostatistics Branch, on the impact of obesity on total mortality in the United States. ■


Michael Thun with Joseph F. Fraumeni, Jr.

—Demetrius Albanes, M.D.