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NATIONAL CANCER INSTITUTE

IN THIS ISSUE

DCP Program Operations Staff Seminar: "Building the Future"

LINDA ("LINDY") WONG AND GLORIA RASBAND

Participants in the third annual DCP Program Operations Staff Seminar: pictured from left to right are (back row) Shannon Brandon, Rhey Palmer, Susan Winer, Christine Donati, Gloria Rasband; (middle row) Linda Gray, Sara Hursen, Jenny Gaegler, Linda ("Lindy") Wong, Barbara Redding; (bottom row) Florence Mann, Joyce Browne, Linda Bremerman, Dianne Gary, Angela Green, Jill Hughes.

The third annual DCP Program Operations Staff (POS) Seminar was held at Baltimore's Inner Harbor on October 7-8, 2002. The purpose of the seminar was to promote growth and development of the POS and to identify ways to continue to improve the operating policies and procedures for the work performed in the Division of Cancer Prevention (DCP). The "real work" module was facilitated by Dr. Rhey Palmer. Participants worked through group discussions to develop recommendations and actions to the issues identified by DCP Coordinating Unit members and key others. The training module was facilitated by Ms. Diane Rhodes from Impact Consulting Services. In preparation for this training, the participants completed a Communication Style Survey – "Managing for Success: Team Building Version." The results were discussed during various team building activities while working on the theme: "Communication plays a vital role in team work and collaboration."

Since January 1999 the mission of the Program Operations Staff Project Team (formerly known as the Non-Scientific Staff Project Team) has been to identify and recommend new and/or improved operating policies and procedures for our Division. That mission continues – into the Future! ■

POS Seminar participants (left to right) Shannon Brandon, Myra Terrell, and Angela Green.

(Left to right) Sara Hursen, Felicia Carr, Tracy Ellis, and Christine Donati at the POS Seminar.

Biometry Research Group's Macro Journey through Microarrays

GRANT IZMIRLIAN

Genomic profiling has recently found successful application in disease subtype identification and in drug discovery. Increasingly, the Division of Cancer Prevention (DCP) is involved with a growing number of cancer prevention studies that use genomic profiling. Correspondingly, members of the Biometry Research Group (BRG), the statistical core of DCP, have spent the past several years learning about these new technologies and, especially, the role that statistical thinking plays in the design and analysis of data arising from genomic profiling studies. A new collaborative effort involving members of the BRG, the U.S. Department of Agriculture (USDA), and DCP's Nutritional Science Research Group has been established over the past six months for the purposes of designing and analyzing studies addressing the interaction between genomic profile and diet. As "training" is the theme of this issue of the **PreventionPOST**, I thought I would take this opportunity to chronicle the BRG's journey from casual bystander to active participant in the design and analysis of gene expression microarray studies.

The spotted complementary DNA microarray, or cDNA microarray for short, was invented by Pat Brown's lab at Stanford University and introduced in their 1995 *Science* article. Our first exposures to the topic at BRG were two seminars held in the spring and summer of 2000. The first, given by Lisa McShane of the Biometric Research Branch (BRB) of NCI's Division of Cancer Treatment and Diagnosis, led off with issues in image quality and proceeded all the way to the final statistical analyses. Most striking was the importance of image quality, and how the statistician needs to be concerned about which segmentation algorithm the investigator has used. Mark Van der Laan of the University of California-Berkeley gave the second lecture on the parametric bootstrap, a tool for conducting formal inference on classes discovered via any clustering algorithm. Aside from the theoretical content, the main message from that talk was the importance of global inference.

Next, in the fall of 2001, we located on the Berkeley Statistics web page a technical report by Sandrine Dudoit, who was a postdoctoral fellow in Pat Brown's lab during the 2000-2001 academic year. Her report discussed the use of class prediction methods (discrimination) to assess the validity/reproducibility of several published reports based upon class discovery (clustering). A collaborative effort consisting of Dudoit, Robert Gentleman of Harvard University, and others, has developed free source software for the pre-processing and analysis of both cDNA and oligonucleotide microarrays. Developers at the Insightful Corporation, producers of the popular S-Plus statistical package, have incorporated this freeware into their new product. Last February several of us took a class, given by representatives from that company through the National Institute's of Health Center for Information Technology (CIT), in which Dudoit's preprocessing techniques

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Presidential Management Intern/Management Intern/Emerging Leaders Program

SUSAN WINER

Does your research group have too many great ideas and no one to implement them? If the answer is "yes," then the Federal Government can meet your needs.

Bright, creative, one-of-a-kind individuals belong to a special group of workers – the Presidential Management Intern/Management Intern/Emerging Leaders Program. These graduate-level individuals compete to join one of these programs and then work in rotations through various areas of government operations, such as budget, administrative and personnel, contracts, and marketing. The intern participates in each rotation from three to nine months, depending upon his or her needs and the needs of the receiving office. In addition, the intern can perform "shadow rotations" lasting only a few days. These are not full-time equivalent positions, nor do the interns receive salary from the offices in which they elect to do their rotations. This is a win-win situation for everyone involved – great ideas are born and implemented and the intern benefits from a valuable mentoring experience. After completion of the 2-year internship, many of these individuals have the opportunity to become a permanent part of the NIH staff.

Carol Storm manages this elite program at the NIH and Christina Bruce is the manager at the NCI. New interns start in July of each year. Ms. Storm schedules a series of oral presentations to be given by offices with potential opportunities for these emerging leaders. Subsequently, each intern schedules interviews with those offices in which they are interested in working. It is the responsibility of the intern to schedule his or her rotations.

Chris Chavis, a Management Intern, recently rotated through the Office of Preventive Oncology and assisted with the Cancer Prevention Fellowship Program's marketing brochures, program web site, and databases. ■

GRAÇA M. DORES AND DOUGLAS L. WEED

Jerome Cornfield
1912-1979

(a*d)/(b*c)†. Cornfield's cross-product was first described in the Journal of the National Cancer Institute in 1951 (1). Today, this mathematical formula serves as the foundation for relative risk estimation from case-control studies. Jerome Cornfield, or "Jerry", as he was best known among colleagues, further enhanced the use of case-control studies by developing the multiple logistic risk function that allowed the concurrent study of several risk factors for a disease. A medical statistician of international acclaim, he was considered a "renaissance man" with unmatched versatility in the theory and application of statistics, epidemiology, clinical trials research, and public health. Cornfield made important contributions not only to cancer research, but also to the understanding of risk factors for heart disease, safety of the polio vaccine, and diabetes.

Born in the Bronx, Cornfield graduated from New York University with a Bachelor of Arts in History and began his career at the U.S. Bureau of Labor and Statistics (BLS) in 1935, where he obtained his only training in statistics and mathematics. At the BLS he made key contributions to the theory of statistical sampling that today serve as the basis for survey and marketing research. In 1947 he joined the Department of Statistical Methods of the U.S. Public Health Service at the National Cancer Institute (NCI). In addition to his contributions to epidemiology, he pioneered work in the design, execution, and analysis of controlled clinical trials and helped to pave the way for the large prevention trials of the 1960s and '70s involving thousands of participants, in contrast to the hundreds that had participated in the 1950s.

Although Cornfield was primarily involved in cardiovascular disease trials, similar approaches are used as a major investigative tool in cancer prevention trials today. Jerry was also one of the major contributors to the Surgeon General's report in 1964 on "Smoking and Health," establishing the causal association between cigarette smoking and lung cancer. He apparently believed that this finding was not just a "statistical association," given that he relinquished his pipe following his studies at NCI. Retiring from the Federal Government in 1967, Cornfield initially took a position at the University of Pittsburgh and subsequently at the George Washington University, where he was able to share his gift for teaching, enhanced by his gentle nature, inquisitive mind, and keen sense of humor.

† **Cornfield's cross-product:**
In epidemiology, when the occurrence of the disease under study is rare (e.g., affects <10% of the population), the odds ratio estimates the relative risk of developing the disease in individuals with a given exposure. A "2-by-2 table" is utilized to arrange the data, as depicted below.

	Cases (disease)	Controls (no disease)
Exposed	a	b
Not Exposed	c	d

In this example, the disease under study is lung cancer and the exposure of interest is tobacco smoke.

a = number of individuals with lung cancer who were exposed to tobacco smoke
b = number of individuals without lung cancer who were exposed to tobacco smoke
c = number of individuals with lung cancer who were not exposed to tobacco smoke
d = number of individuals without lung cancer who were not exposed to tobacco smoke.

The odds ratio is equal to: (a*d)/(b*c). ■

REFERENCES
(1) Cornfield J. A Method of estimating comparative rates from clinical data. Applications to cancer of the lung, breast, and cervix. J Natl Cancer Inst 1951;11:1269-1275.

AWARDS

SUSAN PERKINS AND SUSAN WINER

In December 2002, the following fellows were each presented with a Cancer Prevention Research Training Merit Award: third-year fellow Erik Auguston and fourth-year fellows David Berrigan, Graça Dores, and Jackie Lavigne. This award is presented by the Cancer Prevention Fellowship Program in recognition of outstanding performance as a Cancer Prevention Fellow.

Heather Poetschke Klug, a third-year fellow, received a travel award from the American Society for Photobiology to attend the Annual Meeting in Quebec City, Canada, in July 2002.

Fourth-year fellows David Berrigan and Rachel Stolzenberg-Solomon each successfully competed for a National Institutes of Health (NIH) Fellow Award for Research Excellence (FARE); only twenty-five percent of 828 applicants from all of NIH were selected to receive one of these FARE travel awards.

Third-year fellow Dina Paltoo received the American Association for Cancer Research AFLAC Scholar-in-Training Award at the Frontiers in Cancer Prevention Research meeting in Boston, Massachusetts in October 2002.

Tamy Buckel, a first-year fellow, and Dina Paltoo and Susan Thomas Vadaparampil, third-year fellows, were selected to participate in the New Investigators Workshop at the Annual Meeting of the American Society of Preventive Oncology in Philadelphia, Pennsylvania in March 2003. ■

ON THE PERSONAL SIDE

Best wishes to Maja Zecevic and her husband, Vanja Bogdanovic; and to Ashley Smith and her partner, Jacqueline Ann Neilson, on their recent marriages.

Congratulations to Kenneth Hance and his wife, Dena, on the birth of their son, Austin; to Rachael Stolzenberg-Solomon and her husband, Jeff Solomon, on the birth of their son, Adam Elan; and to Janet Tooze and her husband, Andy, on the birth of their son, Alexander Austin! ■

At the Forefront of Training

SUSAN WINER

The Cancer Prevention Fellowship Program had a busy fall. One hundred and six applications were received, the highest number since the first year of the program in 1987, when 110 applications were submitted. Thirty interviews were scheduled on October 30, 31, and November 1, and seventeen applicants were invited to join the fellowship program. During the three days of interviews, former fellows were invited back to the NCI to give lectures: Paul J. Limburg, M.D., M.P.H., from the Mayo Clinic of Rochester; Karen G. Woodson, Ph.D., M.P.H., from the Center for Cancer Research, NCI; and Rick Boyd, Ed.D., M.S.P.H., from George Washington University. These former fellows presented lectures on their current research and also spoke about the opportunities in the Cancer Prevention Fellowship Program and how the Program has helped them in their careers.

The newest venture in the Cancer Prevention Fellowship Program is the formation of a new career track within the program - the Clinical Cancer Prevention Research Track. Information and in-depth details pertaining to this career opportunity will be included in our new brochures and materials for the Cancer Prevention Fellowship Program - 2004. During the fall interviews, several applicants expressed interest in pursuing the clinical research track.

In our ongoing search for qualified applicants, recruitment for the Cancer Prevention Fellowship Program has been very busy this year. Recent meetings attended include the American Association for Cancer Research premier annual International Meeting on Frontiers in Cancer Prevention Research, American Public Health Association, and the American College of Preventive Medicine. Spring 2003 will take us to the Johns Hopkins Bloomberg School of Public Health Career Fair, the Cancer Health Disparities Summit meeting, and the meetings of several professional societies: American Society for Preventive Oncology, American Association for Cancer Research, Oncology Nursing Society, Experimental Biology, Digestive Diseases Week, and American Society of Clinical Oncology. Assistance in the booth is provided by Cancer Prevention Fellows attending the meetings. ■

Cancer Prevention Fellowship Program

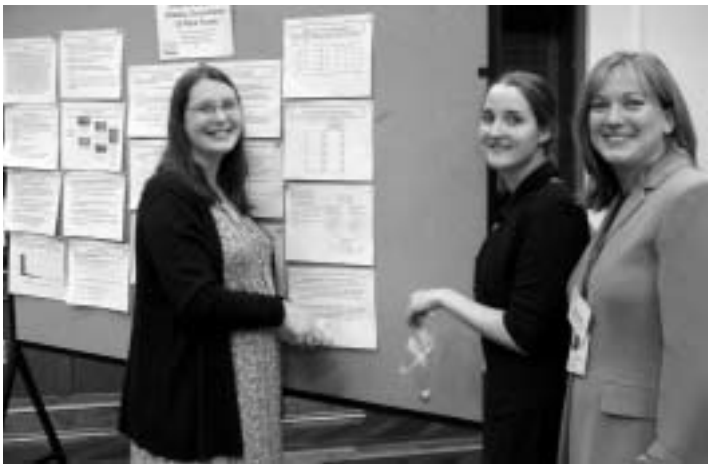
The First Annual Cancer Prevention Fellows' Scientific Symposium

GRAÇA M. DORES

On September 11, 2002 a new tradition was established in the National Cancer Institute's Cancer Prevention Fellowship Program (CPFP) in the Division of Cancer Prevention - the Cancer Prevention Fellows' Scientific Symposium. This inaugural event was held at The Cloisters, located on the campus of the National Institutes of Health in Bethesda, Maryland. In the spirit of commitment to fellowship that dominates the Program, the First Annual Cancer Prevention Fellows' Scientific Symposium promoted scientific exchange and camaraderie among current fellows, former fellows, and the CPFP scientific staff. Following introductory remarks by Dr. Jackie Lavigne, a current Cancer Prevention Fellow, and Dr. Douglas Weed, Director of the CPFP and Chief of the Office of Preventive Oncology, Dr. Peter Greenwald, Director of the Division of Cancer Prevention and the featured speaker, opened the educational session with his talk entitled "Progress in Cancer Prevention." Throughout the day, invited presentations by current fellows encompassed a wide array of topics. Dr. Claudine Kavanaugh discussed the effect of non-steroidal anti-inflammatory drugs on mammary tumor development in a transgenic mouse model; Kerri McGowan Lowrey, Esq., J.D., M.P.H., addressed ethical and legal concerns in advertising for health research; Dr. David Berrigan reviewed Hispanic acculturation and health behavior patterns in the United States; and Dr. Jackie Lavigne shared results of the effects of alcohol intake on serum insulin-like growth factor (IGF) and IGF binding protein levels measured in postmenopausal women.

In her Mid-morning Remarks, Dr. Shine Chang, Associate Director of the CPFP, reflected on the importance of fellowship and cancer prevention science. This was followed by another special highlight of the day, the Career Pathways Workshop, the success of which was attributed to the participation of the former Cancer Prevention Fellows. During the Workshop's Panel Discussion, former fellows each shared personal "pearls of wisdom" gleaned from their career experiences and achievements in the field of cancer prevention. Topics of the ensuing Group Discussion centered on job-seeking, interviewing and negotiating skills, and career opportunities in cancer prevention. The afternoon Poster Session highlighted the fellows' diverse scientific interests, united by their focus on cancer prevention, while senior fellows had the opportunity to describe their ongoing projects and exchange ideas with first- and second-year fellows, former fellows, and CPFP scientific staff. Dr. Stephen Hursting, Deputy Director of the CPFP, provided the Concluding Remarks, summarizing the day's events and the significance of the first symposium. It was a rewarding and enjoyable day, and the Second Annual Cancer Prevention Fellows' Scientific Symposium in 2003 is eagerly awaited by all! ■

Dr. Peter Greenwald, the featured speaker, presents his talk on "Progress in Cancer Prevention."



Cancer Prevention Fellows, (left to right) Janet Tooze, Leah Mechanic, and Kerri McGowan Lowrey, at the afternoon Poster Session.

Former Cancer Prevention Fellows, (left to right) Terryl Hartman, Ernie Hawk, Joanne Dorgan, Stephen Hursting, Sheila Prindiville (not seen) and Susan Rossi, participate in the Career Pathways Workshop. Other panel participants (not shown) were Lisa Colbert, Gary Ellison, Pamela Mink, Ann O'Mara, and Karen Woodson.

The Molecular Prevention Laboratory: Training the Next Generation of Leaders in Cancer Prevention

SUSAN N. PERKINS

Established less than three years ago by Dr. Stephen Hursting, Deputy Director of the Office of Preventive Oncology, Division of Cancer Prevention, the Molecular Prevention Laboratory has several interlocking functions. Its *raison d'être* is to provide Cancer Prevention Fellows experience with the basic techniques of molecular and cellular biology that are being applied to cutting-edge research in the fields of molecular epidemiology, bionutrition, chemoprevention, and translational research. The Laboratory

Dr. Volker Mai, a former fellow now on the faculty of the University of Maryland School of Medicine, continues to collaborate with the Section.

fulfills this mission in several ways. First, it provides logistical support for the laboratory course in which first-year fellows participate as part of the National Cancer Institute Summer Curriculum in Cancer Prevention. Open only to fellows, this eighteen-hour training laboratory uses hands-on exercises to introduce fellows to crucial techniques in current use, such as the polymerase chain reaction (PCR); DNA isolation, mapping, and sequencing; gel electrophoresis and Southern, northern, and western blotting; complementary DNA microarray fabrication and use; and ELISAs and other immunoassays. The goal of this course is not to turn all of the fellows into molecular biologists but rather to give them tangible reference points for understanding how these techniques work.

Second, fellows can use the Molecular Prevention Laboratory to obtain advanced training in laboratory techniques that they then apply to their research in cancer prevention. In the last two years, ten fellows have taken advantage of the opportunities provided by the facility. In practice, these experiences have varied widely. Some fellows have come for short-term training to learn specific techniques, such as cell culture methods. Others, lacking access to a "wet lab" in their primary research group, have used the facility for weeks, months, or longer to process tissue samples, perform immunoassays on human or rodent serum samples, or run PCR reactions and gels, for example.

Third, a number of these fellows have further benefited from the fact that the Laboratory also accommodates the research activities of the Nutrition and Molecular Carcinogenesis Section. As part of the NCI's Laboratory of Biosystems and Cancer (Dr. J. Carl Barrett, Laboratory Chief), this arrangement makes possible intermediate and long-term mentored research experiences for fellows. The Section (http://ccr.cancer.gov/Staff/Staff.asp?StaffID=295) is under the direction of Dr. Hursting, Section Chief and Adjunct Investigator in the Center for Cancer Research, and includes Dr. Susan Perkins, who coordinates Laboratory training and research activities, and Heather Wimbrow, Senior Research Technician. The focus of ongoing work in this Section is the integration of experiments using transgenic animal models and advanced molecular biologic approaches (such as DNA microarrays) with epidemiologic and *in vitro* studies to identify and characterize diet-gene interactions relevant to cancer prevention. Current areas of interest include the mechanisms underlying the energy balance-cancer association, with a particular focus on the role of hormones that may be related to carcinogenesis, such as leptin, insulin-like growth factor (IGF)-1, and IGF binding proteins. Several current fellows and now-former fellows interested in focusing on this area of cancer prevention research have collaborated with the Section on animal experiments designed to investigate these potential mechanisms.

The Molecular Prevention Laboratory is based at the NCI-Frederick campus (http://web.ncifcrf.gov) within Fort Detrick, a military installation in historic Frederick, Maryland. Less than 35 miles north of the Executive Plaza building complex, it is easily reached by a drive up I-270; parking is plentiful.

Heather Wimbrow, senior research technician, and Dr. Lisa Colbert, a former fellow currently at the National Institute on Aging and soon to join the faculty of the University of Wisconsin, perfom Enzyme-Linked Immunosorbent Assays (ELISAs) to measure hormone levels in serum from tumor-prone mice that have been allowed to exercise.

The Molecular Prevention Laboratory continued from page 8

Some current members of the lab (left to right): Heather Wimbrow, Volker Mai, Nomeli Nuñez, Steve Hursting (Section Chief), Jennifer Eng-Wong, Susan Perkins, David Berrigan, and Jackie Lavigne.

Continued progress in cancer prevention and control will require that the next generation of scientists be familiar with a broad range of concepts and techniques in molecular and cellular biology and genetics. Knowledgeable young scientists so equipped will be better prepared to participate in the multidisciplinary research that will most rapidly advance the field. The purpose of the Cancer Prevention Fellowship Program is to train individuals to become leaders in the field of cancer prevention and control; the Molecular Prevention Laboratory is a significant element of the Program. ■

Biometry Research Group's Macro Journey through Microarrays continued from page 2

were presented. Also that month, Rich Simon of the BRB spoke at the DCP Colloquium. In June we attended a course given by Simon's group through CIT.

Another pivotal event in our training occurred last year during our preparations for the Applications of Bioinformatics in Cancer Detection Workshop, in which Richard Fagerstrom, Simon Rosenfeld, and I took part. One of the main goals of that project team was to familiarize itself sufficiently with current research in order to be able to select speakers from among the experts in the field. A second objective was to produce an expository report on the workshop themes for the workshop notebook. This combination of tasks required a deeper investigation and understanding of not only the statistical literature but of the landmark substantive publications as well.

Of course the deepest level of understanding began to develop once we had datasets to analyze. Steve Hursting (Office of Preventive Oncology and the Center for Cancer Research) and his long-time collaborator Tom Wang (USDA) brought me in on the analysis of one of their studies. Soon, Simon Rosenfeld was also participating in a collaboration with Tom Wang and John Milner (Nutritional Science Research Group). Both studies are using cDNA microarrays to assess the effects of dietary components (genistein, a phytoestrogen in soy, in the first case, and diallyl disulfide, an organosulfur compound abundant in garlic, in the second) on gene expression in a human prostate cancer cell line. Analytical tools used in this work are in part taken from the literature and are in part being developed in-house.

The "take away message" from our journey can be summarized in the following points. First, the imaging and data preprocessing steps are of paramount importance. If possible, experimenters should specify a "Data Adaptive" or even "Chen-Dougherty" segmentation algorithm at the time of scanning. With regards to analysis of data, more and more of these studies are hypothesis driven and involve only a few experimental groups with replicates. In our experience, logged relative expressions are quite close to normally distributed, so use of a mixed variances linear model is appropriate. This is in contrast to many of the published findings based upon cluster analysis, which is only appropriate when the number of classes is large and unknown and the experimental design is not hypothesis driven. As a final point, global p-values insure that the false discovery rate is controlled. For example, Bonferonni adjustment means that for a global p-value of 0.05 one assigns a per gene p-value of 0.05 divided by the number of genes. There are other techniques for controlling false discovery rate introduced by Benjamini and Hochberg and applied in this setting by Dudoit.

So far all of the analyses in the BRG have involved cDNA microarrays, but we are beginning to move into Affymetrix oligonucleotide microarrays as well. It is certain that genomic profiling technology will continue to develop and that entirely new types of research questions and experimental techniques will be possible in a few years. More sessions on these topics are planned in the DCP Colloquia Series; see http://www3.cancer.gov/prevention/pob/fellowship/colloquia.html for details. As a final note, we now have an extensive library of references and would be happy to discuss these with interested individuals. ■

DAVE KAUSAL

We would like you to join us in welcoming new staff to DCP:

Dr. Cindy Davis has joined the Nutritional Science Research Group. Cindy received her doctoral degree in Nutritional Sciences with a minor in Human Cancer Biology from the University of Wisconsin-Madison. Before coming to the NCI she had been a Research Nutritionist at the Grand Forks Human Nutrition Research Center where she was examining the effects of trace minerals, particularly selenium and copper, on cancer susceptibility.

Dr. Jason Vourlekis is with the Lung and Upper Aerodigestive Cancer Research Group. Jason comes to NCI from the National Jewish Medical and Research Center and the University of Colorado Health Sciences Center in Denver, Colorado. He is board-certified in pulmonary medicine and critical care medicine. Jason's research interests include pathogenesis of lung cancer, interstitial pulmonary diseases, and experimental therapeutics.

Master Sergeant (Ret) Alfred Brown has joined the Breast and Gynecologic Cancer Research Group. He has accepted a position in DCP as an Administrative Program Assistant. Al is a decorated veteran, who brings a wealth of experience to his new position after having served for more than 20 years in the U. S. Air Force.

Fidelia Acevedo is an Administrative Program Assistant in the Early Detection Research Network . She says she is a recent "transplant" from Arizona and describes herself as a real "person-to-person" employee.

Don Johnsey has joined the Cancer Biomarkers Research Group in DCP as a Program Specialist. He is currently enrolled in the Master of Science Biotechnology Program at Johns Hopkins University concentrating in Bioinformatics. Don has a strong background in clinical reference laboratories, experience with the development and implantation of a global database of antimicrobial resistance, and a history of managing contracts and training individuals that are disabled or disadvantaged.

Dr. Mirta Dansky recently joined the Gastrointestinal and Other Cancers Research Group. Mirta is board certified in Gastroenterology and trained at the University of Buenos Aires in Argentina. Most recently, she worked for the Pan American Health Organization in the area of infectious disease surveillance. She has a special interest in the prevention of hepatocellular and pancreatic cancers.

Charmaine Boswell is new Administrative Program Assistant in the Cancer Biomarkers Research Group. She began her career with the Federal Government as a Stay-In-School employee in 1996, while attending Bowie State University, majoring in Television Production. In 1999 she began working in the Division of Basic Sciences (Center for Cancer Research), where she had been prior to coming to DCP.

BEST WISHES TO:

Carole Watson has left the DCP Administrative Resource Center to transition to the Division of Human Resource Operations, Office of Human Resources, NIH.

Conference Highlight: An International Workshop on Diagnostic Guidelines for Hereditary Nonpolyposis Colorectal Cancer and Microsatellite Instability

ASAD UMAR

The National Cancer Institute (NCI) Division of Cancer Prevention held a workshop in November 1996 entitled "The Intersection of Pathology and Genetics in the Hereditary Nonpolyposis Colorectal Cancer (HNPCC) Syndrome" that led to the standardization of guidelines that are currently known as the Bethesda Criteria. In December 1997 another workshop entitled "The International Workshop on Microsatellite Instability (MSI) and Replication Error (RER) Phenotypes in Cancer Detection and Familial Predisposition" was held in Bethesda, Maryland. Recommendations from this workshop led to the development of five specific microsatellite markers (NCI markers for MSI); these markers have broad utility in several experimental and diagnostic settings. Understanding of MSI and immunohistochemical detection of DNA mismatch repair defects have advanced significantly, and recent findings require a new look at the current issues and guidelines for HNPCC diagnosis.

In order to update the existing Bethesda Criteria and provide a fresh look at the current status of clinical diagnosis of HNPCC and the MSI phenotype, an international workshop on diagnostic guidelines was held in Bethesda on December 11-13, 2002. Cosponsored by NCI's Division of Cancer Prevention, Division of Cancer Control and Population Sciences, and Center for Cancer Research, this workshop convened experts in HNPCC and the MSI phenotype that is associated with familial as well as sporadic forms of colorectal cancer.

Participants included leaders in HNPCC research, such as Henry Lynch, Hans Vasen, Albert de la Chapelle, Paivi Peltomaki, Annika Lindblom, Stanley Hamilton, Jeremy Jass, C. Richard Boland, and J. Carl Barrett, among others. Attendees reviewed and updated existing criteria for HNPCC and MSI and provided recommendations to NCI based on new insights into the disease and its manifestations. Participants also discussed effective strategies for identifying HNPCC mutation carriers, defining the MSI phenotype in cancer, and evaluating correlations between the MSI phenotype and pathological stages of tumor progression and clinical outcome. In addition, they focused on methodological and quality control issues for MSI assays, recommended guidelines for scoring and reproducibility of these assays, and discussed alternative methods for the detection of a mismatch repair defect or MSI phenotype. Finally, a minimum set of MSI markers that would increase sensitivity and specificity of detection of HNPCC and sporadic MSI cancers was recommended. A final draft of these guidelines is currently in preparation and will be published in a nationally recognized biomedical journal for dissemination to the community. ■

PreventionPOST

DCP Newsletter Project Team

THE DCP NEWSLETTER PROJECT TEAM WELCOMES NEW MEMBERS DORIS BROWNE, JACOB KAGAN, DOUG MIDTHUNE, AND ASAD UMAR!

EDITORIAL GROUP: Susan Perkins (Editor-in-Chief), Graça Dores, Grant Izmirlian

DESIGN GROUP: Doris Browne, Dee Sullivan

WEB GROUP: Kathleen Foster, Jacob Kagan, Asad Umar

PRINTING GROUP: Jacob Kagan, Doug Midthune

DISTRIBUTION GROUP: Dave Kausal (photos), Susan Winer, Gloria Rasband

The Clinical Cancer Prevention Research Track: A New Opportunity in the Cancer Prevention Fellowship Program

GRAÇA M. DORES AND DOUGLAS L. WEED

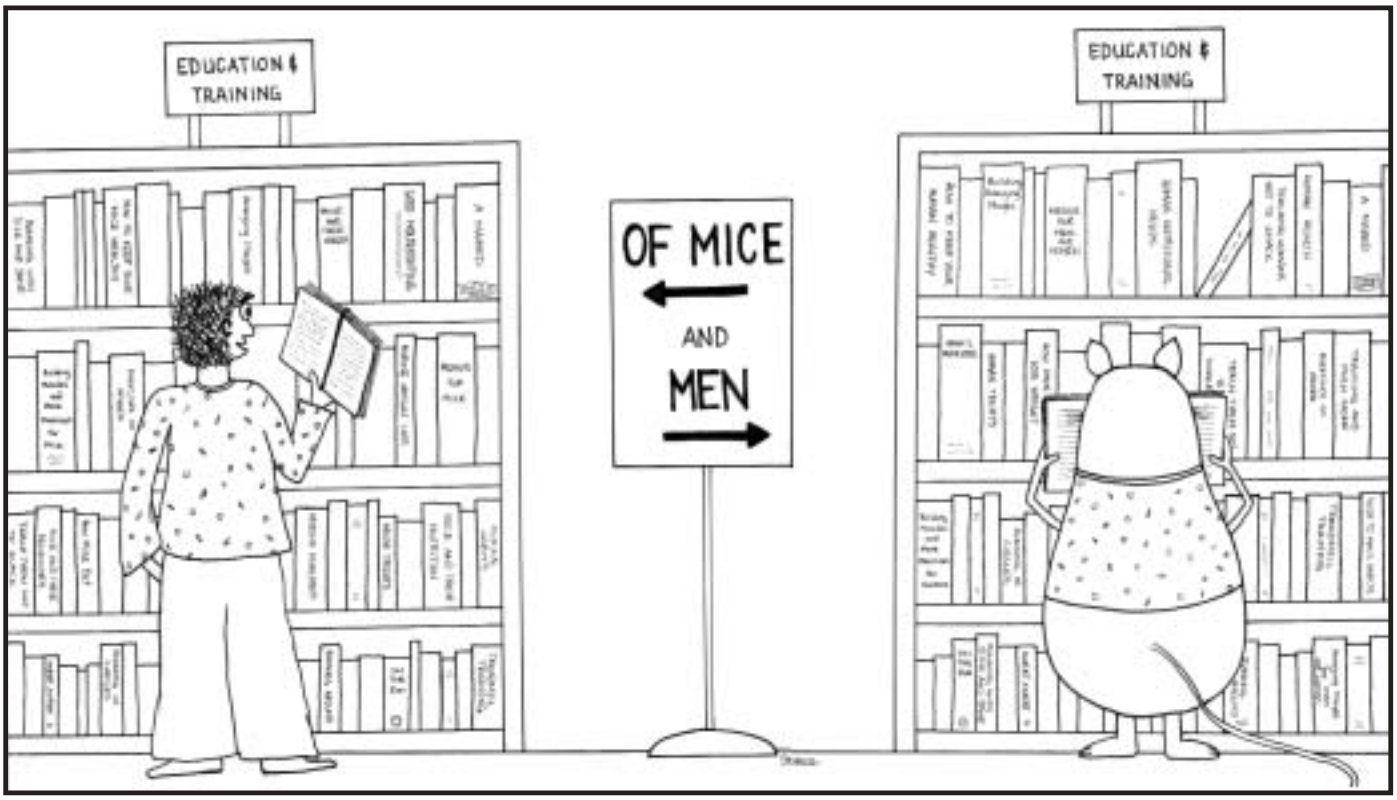
Two years after introducing the Ethics of Prevention and Public Health Track, the Cancer Prevention Fellowship Program (CPFP) announces another new addition - the Clinical Cancer Prevention Research Track. In 2003, physicians, nurses, and other individuals with training in the clinical sciences will have the opportunity to combine their clinical acumen with their interest in cancer prevention research. To enhance training in research methodology and to complement the focus of this track, individuals may pursue a 1-year didactic program to complete either a Master's degree in clinical investigation, clinical research, or clinical epidemiology or a Master of Public Health degree. Eligible fellows may obtain clinical privileges at nearby medical institutions to enable their research endeavors and may also obtain privileges to maintain their clinical skills and state-of-the-art practice principles.

Potential research opportunities include clinical trial investigations, comprising studies of chemopreventive agents, screening and early detection, or other interventions. Alternate pursuits could incorporate clinical outcomes and effectiveness research, study of ethical issues in clinical prevention, or behavioral studies in at-risk populations. Fellows may choose to integrate clinical activities with other cross-disciplinary endeavors, for example, a laboratory experience that would enable investigation of biologic mechanisms of carcinogenesis and identification of potential targets for cancer prevention. Rotations in the Division of Cancer Prevention, to participate in clinical prevention protocol reviews, will further enrich the training experience.

Together with fellows in the parent CPFP and in the Ethics of Prevention and Public Health Track, those in the Clinical Cancer Prevention Research Track will also take part in weekly Fellows' Research Meetings, weekly Colloquia, the Summer Curriculum in Cancer Prevention, the Molecular Prevention Laboratory, and all other hallmark CPFP activities. ■

CARTOON

GRAÇA DORES



The More Things Change...

SUSAN N. PERKINS
Editor-in-Chief

The first issue of the **PreventionPOST** rolled off the presses just three years ago. Under the leadership of its Editor-in-Chief, Doug Weed, the DCP Newsletter Project Team has consistently achieved its goal: to maintain a high-quality newsletter publication for the Division of Cancer Prevention, with regular publication and wide distribution within the National Cancer Institute and for the prevention community at large. Nothing stays the same, of course, and Doug has decided to step down in order to focus on other projects. Fortunately for its new Editor-in-Chief, he is handing over a fine team and a set of established procedures that have made it relatively easy for me to step into those large shoes.

Although the newsletter naturally evolves as new members join the team and bring fresh perspectives and innovative ideas, much of it will stay the same. Regular features bring us: news about people in DCP ("Transitions" and "DCP Awardees"); updates on the Cancer Prevention Fellowship Program ("At the Forefront of Training"); the biographical snippet that I always find wonderfully educational ("History of Cancer Prevention"); and, of course, the cartoon!

A new recurrent feature will be a piece showcasing a DCP program. For this issue the article about the DCP Molecular Prevention Laboratory also ties into the issue's theme of training activities and opportunities. Other theme-related stories that go beyond the obvious (the Cancer Prevention Fellowship Program) include the report on the DCP Program Operations Staff Seminar held this fall and a spotlight on the Presidential Management Intern Program.

Although change is natural, our goal for the newsletter remains unchanged: to continue to publish and distribute a high-quality newsletter for the Division. I welcome suggestions on how we can even better achieve this goal. I invite anyone excited by the prospect of putting his or her ideas into action to join our team; the broader the interests and expertise of the team, the more completely we can cover DCP activities. I am also happy to review pieces from our "emeritus" team members who, like Doug, want to continue to contribute. Thank you for your continued interest in the **PreventionPOST**.

DCP home base: Executive Plaza

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