

PreventionPOST

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NEWSLETTER OF THE NCI DIVISION
OF CANCER PREVENTION

Annual DCP All Hands Seminar: "The Future is in Your Hands"

JUDY SMITH AND DON HENSON



The annual DCP All Hands Seminar at Lansdowne Resort and Conference Center in Virginia

NATIONAL
CANCER
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On May 9-10, 2002 the Lansdowne Resort and Conference Center in Virginia was the setting for the 4th annual Division of Cancer Prevention All Hands Seminar, "*The Future is in Your Hands*." The purpose of the yearly meeting is to share ideas, strengthen working relationships, and explore opportunities for Divisional growth and advancement of prevention science. The session afforded individuals the opportunity to reflect on Division goals, directions and possibilities, and to plan for the future.

Dr. Greenwald opened the seminar with his thoughts on the current state of prevention science and his expectation of DCP as a global

leader in future endeavors. Dr. Rhey Palmer served as the seminar facilitator, leading the group in a variety of team-building and problem-solving exercises, group and self-evaluations, and strategic development activities.

Highlighting the seminar was an address by Dr. Andrew von Eschenbach, the new Director of the NCI. Dr. von Eschenbach shared his vision for the NCI and emphasized the importance of collaborative relationships and partnerships as a way to move prevention to the forefront of the national agenda. His approach focuses on strong leadership skills and the application of a sound business model to translate discovery into clinical practice. In his address to the group he empha-

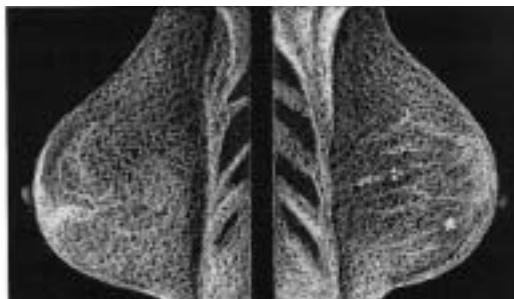
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Mammography Screening for Breast Cancer: The Controversy Continues

KATHLEEN FOSTER

While currently viewed as a routine method for the detection of breast cancer, conventional mammography has been the subject of heated debate over the decades after first gaining popularity in the mid '70s. The most recent cause for discussion resulted from a critique published in *The Lancet* by the authors of a Cochrane Review (O Olsen and PC Gotzsche, *Lancet* 358, 1340-1342, 2001). In this report Danish scientists examined seven large long-term trials that were conducted between the 1960s and the 1980s.

Five of the earliest studies found a benefit from screening. However, the critique cited possible flaws in the way that these early trials were conducted and in the subsequent data analyses. NCI, after serious consideration of the evidence, reaffirmed its recommendation that women have mammograms every one to two years beginning in their forties. The U.S. Preventive Services Task Force, after more than two years of study, took a



similar position.

Up until World War I there were no methods in place to detect breast cancer before it presented itself as a hard mass in the breast, in some instances accompanied by ominous skin changes and nipple retraction.

However, technology was poised to impact the diagnosis of a disease that has plagued women since ancient times. Roentgen discovered the x-ray in 1895, and by 1913 Salomon in Germany had used x-rays to examine 3000 amputated breasts. Through this he was able to differentiate nodular types from other forms of breast cancer and to make note of microcalcifications. Gershon-Cohen of Philadelphia studied breast x-rays in an effort to determine mammary patterns and in 1948 was the first to show the feasibility of detecting non-palpable cancers. Progress was slow until 1962 when Egan, a radiologist at M.D. Anderson Hospital in Texas, reported on a study of 2,522 mammograms. These were inter-

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DCP Changes Funding Mechanism for Contracts

KATHLEEN FOSTER

DCP is updating its way of conducting business with scientific investigators interested in chemoprevention. As the time approaches for the old contract mechanism to expire, a novel and streamlined system has been formulated in order to enhance the success of the clinical trial process. The new Request for Proposals (RFP), titled "Phase I and Phase II Clinical Trials of Cancer Chemopreventive Agents," will replace the former Master Agreement Holder mechanism for conducting these initial phase drug trials. The closing date for response to this RFP is August 15, 2002.

The objective of the new RFP is to conduct multiple, early phase clinical trials of DCP-sponsored cancer prevention agents. An additional goal is to establish an infrastructure consisting of one or more collaborating institutions that will perform these studies. Chemoprevention

drugs to be evaluated in these clinical trials will be commercially available agents, study drugs developed by the NCI, or those provided by the pharmaceutical industry to NCI for collaborative usage.

DCP intends to award multiple contracts under this program. Each Contractor will be able to initiate from one to five clinical trials per year. The size of each trial will vary depending on the phase of drug development and the organ site under study. This new mechanism encourages collaboration among investigators. Offerors must be well organized and have the capability of recruiting an adequate number of participants in order to facilitate prompt completion of trials. Accrual to all trials will be closely monitored. As a further incentive, Contractors will have the flexibility to subcontract with investigators at additional sites who can consequently provide specific technical expertise for biomarker studies. ■

Vaccination and Cancer Prevention

RON LUBET

In 1967 smallpox killed roughly 2,000,000 persons worldwide. During the conquest of the Indian populations of North and South America between 1550 and 1850, smallpox, a European disease, killed at least three times as many as were killed with the sword and the gun. Yet today, due to immunization, smallpox has virtually been eliminated.

Employing the immune response in the realm of cancer prevention and treatment has been a major hope for at least 40 years. However, problems associated with this approach include 1) a limited number of cancer-specific proteins; and 2) the fact that most cancer-specific proteins are not totally new to the individual. Therefore, an individual is likely to be “tolerant” or “immunologically unresponsive” to the protein of interest. Nevertheless, recent advances in identifying proteins expressed primarily in cancers, as well as discoveries in immunology that may allow one to “break tolerance,” have resurrected the hopes for cancer vaccines.

Immunization Against Infection with Human Papillomavirus (HPV)

HPV has been implicated in cancers of the larynx, anus, and skin in immunosuppressed patients. However, its

clearest role is in cervical cancer, which kills roughly 200,000 women worldwide on an annual basis. In an attempt to block HPV infection, a trial directed by NCI intramural investigators will give young, sexually active women a vaccine consisting of proteins from the outer coat (capsid) of the virus (JT Schiller and DR Lowy, *Expert Opin. Biol. Ther.* 1, 571-581, 2001). This vaccine does not include any other viral proteins or viral nucleic acids, in contrast to smallpox or polio vaccines, which employ killed or attenuated whole virus. Success in this trial should affect cervical cancer incidence, morbidity, and mortality in 15 to 20 years. A vaccine for women already infected with HPV and with cervical lesions might be achieved by immunizing against specific viral proteins (e.g., E6 and E7) that are expressed in HPV-transformed cells.

Carcinoembryonic Antigen (CEA)

The CEA protein is expressed during fetal development, in the gastrointestinal (GI) tract, and in various endodermally derived tumors. Thus, a high percentage of GI tumors (colon, stomach, esophagus), ovarian cancers, and non-small cell lung cancers and perhaps 50% of breast malignancies express CEA. In order for a substantial immunologic response against a protein antigen to occur,

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PreventionPOST



DCP Newsletter Project Team

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IN MEMORIAM

The Cancer Prevention Fellowship Program lost an outstanding young investigator in the field of cervical cancer prevention. **Kathleen Jennings-Dozier** passed away on May 16, 2002.

Majoring in nursing, Kathleen received her Bachelor of Science degree at Rutgers University and her Master of Science degree at Hampton University. After obtaining her doctorate at the University of Pennsylvania, Kathleen was accepted to the Cancer Prevention Fellowship Program, starting in the sum-

mer of 1997. Subsequent to completion of a Master of Public Health degree, she continued her research off-site at Thomas Jefferson University, focusing on cervical cancer prevention in public housing residents. In the summer of 2000, Kathleen was awarded the Cancer Prevention Research Training Merit Award for outstanding performance as a Cancer Prevention Fellow. At the completion of her fellowship, she joined the faculty of MCP Hahnemann University as an Associate Professor.

AWARDS

SUSAN PERKINS

Lila J. Finney, a first-year fellow, received the Society of Behavioral Medicine's Outstanding Dissertation Award in April 2002.

Mollie Howerton, a third-year fellow, won second place for her poster, "Community-based Prostate Cancer Screening: Strategies for Recruitment," at the American Society of Preventive Oncology Annual Meeting in March 2002.

Claudine Kavanaugh, a third-year fellow, was the recipient of the American Association for Cancer Research Scholar in Training Award at the American Association for Cancer Research/NCI meeting, "Molecular Targets and Cancer Therapeutics: Discovery, Biology, and Clinical Applications," in October 2001.

La Creis Renee Kidd, a second-year fellow, was honored with two awards this winter: the New Investigators Award by the American Society of Preventive Oncology and the Minority Scholar Award in Cancer Research by the American Association for Cancer Research.

Dina N. Paltoo, a second-year fellow, received the American Association for Cancer Research Minority Scholar Award in Cancer Research to attend the April 2002 Annual Meeting in San Francisco. She was also nominated for Who's Who Among America's Teachers, 2002, by one of her former students.

Rachael Stolzenberg-Solomon, a third-year fellow, was presented with an award in April 2002 by Drs. von Eschenbach and Fraumeni in recognition of the best paper published in 2001 by a postdoctoral fellow in the Division of Cancer Epidemiology and Genetics. The title of her paper was, "*Helicobacter pylori* Seropositivity as a Risk Factor for Pancreatic Cancer," published in the *Journal of the National Cancer Institute*, 93:937-941, 2001. ■



Cancer Prevention Fellowship Program

ON THE PERSONAL SIDE

Best wishes to Lila and Derek Finney on the birth of their son, Julian James, born on March 19, 2002.

Congratulations to Susan Thomas and Matt Vadaparampil on their recent marriage. ■

At the Forefront of Training

SUSAN WINER

Eleven fellows have just returned from receiving their Master of Public Health degree. Seven graduated from Johns Hopkins Bloomberg School of Public Health - Hala Azzam, PhD, MPH; Dilyara Barzani, MD, MS, MPH; Amanda Greene, PhD, MSN, MPH; Qing Lan, MD, MS, MPH; Nomeli Nunez, PhD, MPH; Arti Patel, PhD, MPH; and Shanita Williams-Brown, PhD, RN, CS-FNP, MPH. This year two fellows graduated from the Harvard School of Public Health - Lila Finney, PhD, MPH and Kay Wanke, PhD, MPH. Somdat Mohabir, PhD, MPH graduated from New York Medical College and Whitney Randolph, PhD, MPH graduated from University of North Carolina-Chapel Hill.

The Summer Curriculum in Cancer Prevention will begin on July 1, 2002. Almost 100 researchers and clinicians will be attending this 17th annual, six-week, summer lecture series. The NCI/All Ireland Consortium is sponsoring 10 students and the Office of International Affairs/NCI is sponsoring 17 researchers from several countries, including Argentina, Costa Rica, Egypt, Ghana, India, Iran, Jordan, Kenya, Korea, Malaysia, Nepal, Spain, Turkey, and Vietnam. Scientists and clinicians from Australia, Canada, Italy, Japan, South Korea and Thailand make up the remainder of attendees in addition to current second-year Cancer Prevention Fellows and other NCI researchers who have enrolled in the course.

Recruitment for the Cancer Prevention Fellowship Program has been very busy this year and the recruitment booth has an attractive new display. Recent meetings attended include the American College of Preventive Medicine, Johns Hopkins Bloomberg School of Public Health career fair, American Society for Preventive Oncology, Association of Teachers for Preventive Medicine, American Association for Cancer Research, Oncology Nursing Society, Federation of American Societies for Experimental Biology, Society of Teachers of Family Medicine, NCI-Frederick/Ft. Detrick Spring Research Festival, American Society of Clinical Oncology, Society for Epidemiologic Research and the Cancer Health Disparities Summit. Assistance in the booth is provided by Cancer Prevention Fellows attending the meetings. ■



Dr. Peter Greenwald

Congratulations to **Dr. Peter Greenwald** (OD) for being selected to receive the prestigious American Cancer Society Award at the American Society of Clinical Oncology Annual Meeting in Orlando, Florida in May 2002. The award was presented to Dr. Greenwald in recognition

of his “unwavering leadership in establishing the science of cancer prevention and for building a national clinical research program in cancer prevention.”



Dr. Stephen Hursting

The American Society for Nutritional Sciences honored **Dr. Stephen Hursting** (OPO) with the Bio-Serv Award in Experimental Animal Nutrition at the Federation of American Societies for Experimental Biology meeting held in New Orleans, Louisiana in April 2002.

This award is given for “meritorious research in nutrition” and was presented to Dr. Hursting “in recognition of his creative use of molecular techniques, including transgenic mouse models, to study the potential role of nutrition in cancer prevention.”



Dr. Joseph Kelaghan

In recognition of his contributions as Acting Chief of the Community Oncology and Prevention Trials Research Group, **Dr. Joseph Kelaghan** (COPTRG) was awarded the Public Health Service Commendation Medal in the fall of 2001.

At this year’s annual DCP All Hands Seminar in May, individuals and project teams were recognized for their contributions to cancer prevention research, leadership, and distinguished service. Individual awards were presented to **Dr. Diane Solomon** (BGCRG), **Dr. Ernie Hawk** (GICRG), and **Dr. Doug Weed** (OPO), with a special award extended to **Dr. Peter Greenwald** (OD). The achievements of the **Chemoprevention of Tobacco-Related Cancers in Former Smokers Project Team**, the **Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO) Project Team**, the **Program Operations Staff Project Team**, and the **Staff Orientation Project Team** were also acknowledged (please see page 1 for more details).

Felicitations to all on these laudable achievements! ■

IN MEMORIAM

Judy Binstock
1935-2002

DCP was deeply saddened by the sudden passing of our dear colleague, Judy Binstock, on March 15, 2002. Judy was a dynamic and delightful individual and nurturing friend to us all.

Judy’s NCI career began in 1981 when she joined the Office of the Director (OD), Division of Resources, Centers and Community Activities. She worked as a clerk-typist under the direction of Joyce Heinonen, with Dr. Peter Greenwald as Director. In November 1982, Judy left OD to work for Dr. Win Malone as Branch Secretary in the Chemoprevention Branch, in the newly formed Division of Cancer Prevention and Control (DCPC). She worked for Dr. Malone for 12 years. In February 1994, Judy became secretary to the Executive Secretary, DCPC, Board of Scientific

Counselors, with Linda Bremerman as the Executive Secretary. In 1996, Judy was reassigned to work for Dr. Diane Solomon. At the time of her death, Judy was the secretary to Dr. Karen Johnson and the Breast and Gynecological Cancer Research Group.

A memorial service was held April 12, 2002 in the Executive Plaza North Conference Center to remember and celebrate the life of our colleague. Supervisors, colleagues, and close friends shared stories, photos, and memories of one who will not be forgotten. Among those participating in the service were Lindy Wong, Dr. Peter Greenwald, Dr. Karen Johnson, Dr. Diane Solomon, Dr. Win Malone, Kathleen Foster, Laura Egan, Marilyn Goldberg, Dr. Ron Lubet, Dr. Marjorie Perloff, Dr. Vernon Steele, and Dan Kaplan. Judy was well-loved and respected by all in the Division and will be greatly missed. ■

DCP's Biometry Research Group: What Do We Do?

GRANT IZMIRLIAN

What do the scientists in the Biometry Research Group do? Much the same thing that biostatisticians (plus one epidemiologist) at any world-class research unit do: a mixture of service activities, collaborative research, and individual research. While these three motifs are well defined and to some extent exclusive, there is a high degree of overlap and cross-fertilization between them.

For example, in the collaborative research/service arena, there is the highly visible Prostate, Lung, Colorectal and Ovarian Cancer Screening (PLCO) Trial. Our chief, Phil Prorok, is co-principal investigator with John Gohagan of the Early Detection Research Group (EDRG). Many of us in BRG are involved with the operations and analysis of data from this trial. On the immediate horizon are several manuscripts presenting the baseline population characteristics and screening findings for each of the respective organ sites. Each organ site paper has as its primary author someone from the appropriate field of oncology, while one or two of us on the organ-specific subcommittees will provide statistical expertise. Other organ-specific research projects arising from the PLCO trial may originate from these oncologists at the screening centers and result in collaborative work within BRG. Dave Levin and Grant Izmirlian serve on the prostate subcommittee, Pam Marcus and Ping Hu serve on the lung subcommittee, and Richard Fagerstrom and Jian-Lun Xu serve on the ovarian subcommittee. Also on the horizon is an interim analysis of the PLCO trial primary outcome data. Group sequential methods and stochastic curtailment methods will both be used to check the primary endpoint (organ-specific cancer mortality) in the intervention versus control arms for any indication, affirmative or null, of early stopping. Richard Fagerstrom, Grant Izmirlian, and Phil Prorok are involved in this project. Other PLCO-related work includes Grant Izmirlian's analyses of quality assurance in the assays of prostate-specific antigen (PSA) and cancer antigen 125 (CA125). The above-mentioned work has spawned several other projects. Jian-Lun Xu is comparing several published methods against his own methods for quantifying and estimating the false positive rate in a trial of repeat screening.

Richard, Grant, and Phil will be benchmarking early stopping methods on several well-known and completed large screening trials such as the Health Insurance Plan (HIP) study, the Minnesota Fecal Occult Blood (FOB) trial, and the Mayo Lung Screening Study. Ping Hu has analyzed data comparing chest x-ray readings at PLCO screening centers.

Other important screening trials are being planned and coordinated in collaboration with EDRG. With the advent of spiral CT (radial computed tomography), the Lung Screening Study, a pilot, was conducted in order to gauge the feasibility of conducting a full-scale trial. The results of that pilot study are nearing publication. The National Lung Screening Trial (NLST) is now underway. Richard Fagerstrom and Pam Marcus have made major contributions to this trial. Also involved is Ping Hu, who provides additional statistical support.

While research dealing with screening is a major component of the work done at BRG, several investigators are making a big impact on the interplay between nutritional epidemiology and cancer. Blossom Patterson works with data from several trials on the preventive effects of dietary selenium. Victor Kipnis, Doug Midthune, and several collaborators from other organizations study the consequences of dietary measurement error in studies of diet and cancer. One completed investigation, the Observing Protein and Energy Nutrition (OPEN) study, was a study of two dietary assessment instruments conducted alongside biomarkers for long-term energy and protein intake. Results indicate that dietary risk factors over two-fold can easily be attenuated out of significance by a very plausible mechanism of measurement error in reported dietary intake.

Simon Rosenfeld collaborates with Victor and Doug on the nutritional epidemiologic work and is also interested in the issue of model selection and model misspecification. He has also been studying molecular biology and the analysis of microarray data. Together with Richard Fagerstrom and Grant Izmirlian he serves on the Applications of Biomarkers to Cancer Data (ABCD) project team. As in many parts of the Division, there is a strong impetus towards involvement with molecular biology and microarray data analysis. Currently, several of us are collaborating with Stephen

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Hursting of the Office of Preventive Oncology on the analysis of data from knockout mice and human cancer cell lines. Several of the Cancer Prevention Fellows with interest in statistical research are involved in this project as well as other ongoing studies at BRG. Janet Tooze, our current Cancer Prevention Fellow, was preceded by Lori Dodd, now on staff in the Division of Cancer Treatment and Diagnosis. Also of note is the fact that Pam Marcus started out as a Cancer Prevention Fellow.

Our trialist, Vance Berger, is very interested in pitfalls in the design and conduct of randomized clinical trials. His work deals with exact inference and selection bias. Together with the other members of BRG, Don Corle and Blossom Patterson, he is at work applying some of these ideas to other studies arising out of collaborative efforts at BRG. Don Corle coordinates BRG's statistical review of all of the concepts and protocols that originate in the Division's Protocol Information Office. Each of the BRG scientists serves as a statistical reviewer on three to ten protocols per year. Most of the protocols are from the Community

Clinical Oncology Program and deal with adjuvant therapy, but there are others, such as the periodic review of chemoprevention trial protocols.

Stuart Baker is our local expert in missing data problems. His projects deal with estimating sensitivity and lead time in screening trials, historical controls, missing-by-design trials, and surrogate endpoints. For example, the missing-by-design work has applications in the meta-analysis of the non-controlled clinical trials. Stuart's work with surrogate endpoints addresses important issues in prevention studies and has spawned a discussion group that includes Victor Kipnis and Grant Izmirlian.

Perhaps I have just scratched the surface by giving such a small snapshot of what goes on at BRG. One thing is clear: that service/collaboration and individual research are symbiotic components of our work here. ■

HISTORY OF CANCER PREVENTION

DOUGLAS L. WEED

Sylvester Graham

1794-1851



The names of most staple foods are straightforward and simple, providing us with clear descriptions of what we are about to eat. White bread. Green beans. Artichoke hearts. Peanut butter. A "dish", on the other hand, comprised of several different single foods, is more likely to have a name that reflects its origins or its creator; Waldorf and Cobb salads are good examples, as is General Tso's Chicken found on every Chinese Restaurant bargain lunch menu. What is exceedingly rare is a simple food that still carries its creator's name with it with every bite. Like the lowly graham cracker that graces the bottom of cream pies and s'mores. Its creator was born over 200 years ago.

Sylvester Graham was the 17th child of a Connecticut preacher who, with little formal training, followed in his

father's footsteps, and launched a career as a traveling evangelist. Crusader may be a better description of his approach to saving souls. He railed against the evils of strong drink, sexual excess, and the "unnatural stimulants" of rich foods, meats, and condiments. Prime among his dietary targets were baked goods made from highly refined white flour. Graham became famous, touting vegetarianism and whole-grain brown wheat flour, later nicknamed "graham flour." In the 1840s, Oberlin College tried unsuccessfully to keep their undergraduate students happy on a diet of graham crackers and water. And by some peculiar stroke of fate, these crackers remain with us today, a reminder that diet has long been considered an important avenue to better health, if not spiritual salvation. Today whole grain foods, high in fiber and vitamins, continue to be examined for their chemopreventive properties. ■

sized that "the individual can succeed, but only the team can win." Dr. von Eschenbach answered questions from the group relating to issues of health disparities, interdisciplinary approaches to problem solving, balancing the NCI portfolio, and developing a closer relationship between cancer treatment and cancer prevention.

Working in small groups, one of the initial activities of the seminar charged individuals with identifying their area of expertise and professional contribution to DCP. The results were then discussed in the context of the Division's working groups. A framework emerged that reflected the cohesive spirit and impact of individuals on the Division's mission. Later in the day, exercises were conducted that helped participants formulate the vision for DCP in the context of the global cancer prevention agenda.

As a closing activity, small groups identified and shared priority items for the future. Recommendations included the development of a scientific strategic plan, addition of a bioinformatics project team, integration and centralization of bio-marker activities and projects within the Division, development of new partnerships across agencies, integration of Community Clinical Oncology Programs (CCOPs) into research group activities, and exploration of potential interactions with the cancer genetics networks.

An awards ceremony was held at the end of the first day to recognize and honor individuals and project teams. There were three award categories: Distinguished Achievement in Cancer Prevention Research Awards, Division of Cancer Prevention Leadership Awards, and Distinguished Service Awards.



Dr. Diane Solomon receives Distinguished Achievement in Cancer Prevention Research Award



Dr. Ernie Hawk receives Distinguished Achievement in Cancer Prevention Research Award

Dr. Diane Solomon (BGCRG) received the Distinguished Achievement in Cancer Prevention Research Award for her extensive contributions to the understanding of cervical neoplasia, advances in cervical screening, and outstanding efforts with the ASCUS/LSIL Triage Study (ALTS). Also honored with the Distinguished Achievement in Cancer Prevention Research Award was Dr. Ernie Hawk (GICRG) for his accomplishments in the understanding of cyclooxygenase-2 (COX-2) as a prevention target and translation to clinical practice.



Dr. Doug Weed receives Division of Cancer Prevention Leadership Award

The Division of Cancer Prevention Leadership Award, given in recognition of exemplary leadership and service to cancer prevention, was presented to Dr. Doug Weed (OPO). Dr. Greenwald cited Dr. Weed's outstanding leadership and organizational capabilities, and dedication to the mission of the Division and to training the next generation of prevention scientists.



Dr. Vernon Steele accepts Distinguished Service Award for the Chemoprevention of Tobacco-Related Cancers in Former Smokers Project Team



Drs. Phil Prorok and John Gohagan receive Distinguished Service Award for the PLCO Project Team

Distinguished Service Awards were presented to two scientific project teams that address issues critical to the research objectives of DCP, demonstrate collaborative effort through open and active communication, and are responsive to team management. Awardees were Drs. Eva Szabo (LUACRG) and Vernon Steele (CADRG) for the Chemoprevention of Tobacco-Related Cancers in Former Smokers Project Team, and Drs. John Gohagan (EDRG) and



Lindy Wong accepts Distinguished Service Award for the Program Operation Staff Project Team



Jenny Gaegler accepts Distinguished Service Award for the Staff Orientation Project Team

Phil Prorok (BRG) for the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO).

Two project teams received Distinguished Service Awards for addressing issues critical to the Division's infrastructure, operations, and special projects. Awardees were Lindy Wong (COP-TRG) and the Program Operations Staff Project Team, and Jenny Gaegler (BRG) and the Staff Orientation Project Team.

A special award was presented to Dr. Greenwald by the Division members in recognition of his many contributions, vision, and leadership in the field of cancer prevention. ■

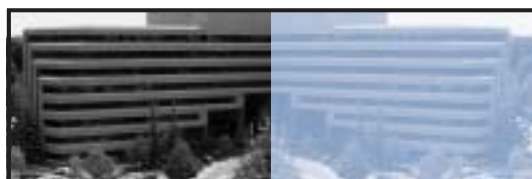
antigen-presenting cells (e.g., dendritic cells, macrophages) must capture the antigen and present it to T-cells and their receptors. A simultaneous co-stimulatory signal is required for T-cell activation, and the activated T-cells release immune stimulatory factors, e.g., interleukin-2 and interferon. Investigators at the NCI have been working on an immunization protocol against CEA that stimulates an immune response by combining a recombinant avian poxvirus containing CEA and three co-stimulatory molecules with a second poxvirus expressing granulocyte-macrophage colony-stimulating factor (GM-CSF) to further enhance the immune response (DW Grosenbach, *et al.*, *Cancer Res.* 61, 4497-4505, 2001). Employing this vaccine strategy, these researchers have elicited a substantial immune response to CEA in humans and in animal models. In animal studies this immunization is effective in cancer prevention and in therapy of colon cancer and seems to overcome "tolerance." Preliminary results in humans with cancer also appear promising (M von Mehren, *et al.*, *Clin. Cancer Res.* 6, 2219-2228, 2000).

Vaccination Against HER-2/neu Employing Specific Peptides

The HER-2/*neu* protein is a member of the epidermal growth factor receptor family and is involved in signal transduction and cell growth. *Neu* is overexpressed in a variety of tumors including breast, ovary, and prostate cancers. Recently Herceptin, a monoclonal antibody directed against *neu*, has been shown to be effective in the treatment of advanced breast cancers that highly overexpress *neu*. Herceptin works through passive immunity: antibodies or cytotoxic T-cells not produced by the host are injected into the patient in order to kill cancer cells. In contrast, the examples for HPV and CEA employ active immunization, whereby the host develops her/his own immunologic response (e.g., antibodies or cytotoxic T-cells) to the tumor-expressed protein. The two vaccination strategies discussed

for CEA and HPV utilize intact proteins, whereas this third approach uses synthetic peptides (fragments of a complete protein, e.g., *neu*) for immunization. Development of specific peptides involves determining sequences of amino acids from the immunizing protein (e.g., *neu*) that will preferentially form complexes with the major antigen-presenting molecules, major histocompatibility complex classes I and II. Since different groups of individuals have different antigen-presenting molecules, scientists can optimize the specific peptides to be employed for immunization of specific groups of individuals. The use of these specific antigenic peptides in humans has only recently begun in therapy (H Bernhard, *et al.*, *Endocr. Relat. Cancer* 9, 33-44, 2002). The fact that strong, long-term immunologic responses have been observed in persons with cancer appears promising. The possibility of using this vaccine in cancer prevention is particularly appealing, and this approach has already proven to be successful in animals.

These three examples illustrate some of the varied potential approaches to the use of vaccination in the field of cancer. HPV-related studies in cervical cancer represent a classic approach since the vaccine will attempt to block infection by the major etiologic agent, HPV. Although the other approaches utilized to elicit a therapeutic immune response in individuals with cancer are more difficult to achieve, initial studies appear hopeful. Studies in the area of cancer prevention have not yet been undertaken on a large scale despite the fact that vaccines may be a particularly promising approach. Even if successful, vaccination still raises questions relevant to most preventive or therapeutic strategies: 1) Must different vaccines be developed for cancers in different organs? 2) Must different vaccines be developed for specific histologic types of cancer within a specific organ? and 3) Are significant side effects likely? Nevertheless, the vaccination field appears ripe for continued and more detailed studies and may well play a major role in cancer prevention in the future. ■



DCP home base: Executive Plaza

preted independently of clinical findings, and demonstrated the ability to differentiate between benign and malignant tumors. 1963 brought the Health Insurance Plan (HIP) study, the first randomized trial using mammographic screening of healthy women. After 7 years of follow-up, there was a 30% reduction in the breast cancer mortality rate in the study group relative to the control group. A reduction in breast cancer mortality rate of 23% was still observed after 18 years of follow-up. This early detection effort was followed up with the NCI-funded Breast Cancer Detection and Demonstration Project (BCDDP) in 1973. Both of these studies illustrated the ability of mammography to detect non-palpable cancers. In data collected by the BCDDP, the relative contribution of mammography alone was 41.6% of the cancers found. Of these cancers, 59% were non-infiltrating.

It was during this era of mass screening that controversy first erupted. The BCDDP was criticized for not being designed as a randomized clinical trial, thus having no pre-selected comparison group. Instead, its goal was to get the word out to both the medical profession and the public about techniques for the early detection of breast cancer. In this it was successful, screening over 280,000 women for the initial visit, with 51.7% completing the 5-year program. In fact this program opened the door to many other issues such as radiation dosage and safety, leading the way for improved monitoring of mammography facilities and dose reduction. Another crucial issue that evolved was the treatment of early lesions, both non-infiltrating and pre-malignant. These

management questions have since paved the way for a better understanding of the cancer process and in the decreased need for invasive breast surgery. The importance of clinical breast exam in conjunction with a mammogram was also illustrated. The combined modalities of physical exam with mammography resulted in increased rates of detection as each modality contributed cases not detected by the other.

This latest debate serves to illustrate the need for careful scientific evaluation of new screening technologies. Dr. Peter Greenwald, Director of the Division of Cancer Prevention, stated that NCI scientists are modeling the effect of screening on stage-specific incidence. In the U.S. diagnosis of late-stage breast cancer has decreased, and early-stage cancer has increased. Breast cancer mortality has declined 13% since 1990.

The hypothesis is that disease is increasingly being detected at a point where treatments are more likely to be effective. In support of this, statistical modeling shows a clear benefit from mammography and from recent improvements in treatment for breast cancer.

NCI Director, Andrew von Eschenbach, MD, has said, "Early detection of cancer saves lives and we continue to recommend mammography for women 40 and older." However, "it is absolutely essential to look beyond the debate over the limitations of current data and to accelerate the development of better screening tools...While we seek improved methods of diagnosis and treatment of breast cancer, today mammography remains an important part of our efforts to save lives through early detection." ■

Annual Lecture on Cancer Prevention

SUSAN WINER



Dr. Leslie Bernstein, American Family Life Assurance Company, Chair in Cancer Research, Professor of Preventive Medicine, and Senior Associate Dean of Faculty Affairs, Keck School of Medicine of the University of Southern California in Los Angeles, CA will be the speaker at

the third Annual Advances in Cancer Prevention Lecture. The title of her lecture is "***Cancer Prevention: Opportunities for Action.***" This keynote lecture is part of the Summer Curriculum on Cancer Prevention and will be held on Thursday, August 1, 2002, 3:00 PM in the Lister Hill Auditorium on the main NIH campus. A reception will be held following the lecture. ■

DEE SULLIVAN

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



Stephen Carrington, M.A.
Program Analyst,
Nutrition Science Research Group
From the Baltimore City Health Department



Margaret House, R.N., B.S.N., O.C.N.
Nurse Clinician,
Prostate and Urologic Cancers Research Group
From Ashbury Methodist Village Retirement
Community



Sara Hursen
Secretary,
Office of the Director
From Division of Cancer Epidemiology and
Genetics



Jacob Kagan, Ph.D.
Program Director,
Cancer Biomarkers Research Group
From M.D. Anderson Cancer Center



Guillermo Marquez, Ph.D.
Special Expert,
Early Detection Research Group
From Texas A & M



Myra Terrell
Administrative Program Assistant,
Protocol Information Office
From the private sector

BEST WISHES TO:

Nicole Harris, Lung and Upper
Aerodigestive Cancer Research Group,
who joined the National Institute of Child
Health and Human Development.

Andrew Hruszkewycz, Prostate and
Urologic Cancer Research Group, who
joined the Organ Systems Branch, NCI.

Lora Kutkat, Cancer Biomarkers Research
Group, who joined the Office of Science
Policy and Planning, Office for Special
Populations, NIH.

Claudette Varricchio, Community Oncology
and Preventive Trials Research Group, who
joined the National Institute of Nursing
Research as Director for Extramural
Research.

Thea Kalebic, Lung and Upper
Aerodigestive Cancer Research Group,
who joined Novartis Pharmaceuticals.

Mirror on Wall Street

DOUGLAS L. WEED
Editor-in-Chief



DCP leadership explores PROFILOR to determine strengths and weaknesses

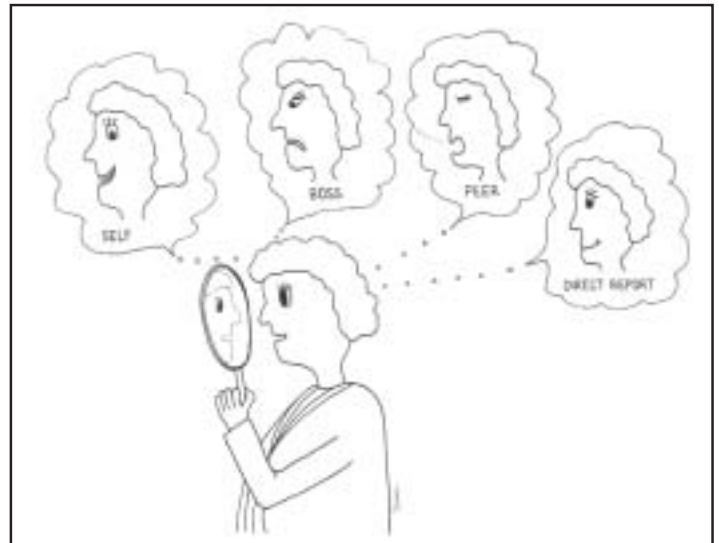
Several months ago, the leadership of the Division undertook an exercise designed to elicit feedback on managerial skills and competencies from the people with whom and for whom they work. The exercise, sometimes referred to as a “360,” is sort of like looking in the mirror Ms. White and her stepmother made famous years ago in the full-length feature for which Mr. Disney won an Oscar. By design, it tells you in brutally frank language how you are perceived by others. The “360,” otherwise known by its copyrighted name, PROFILOR, is a long questionnaire addressing issues of leadership, interpersonal relations, communication, motivation, and organizational knowledge, to name several. Wall Street business speak, in other words.

For each of us who participated, the questionnaire was distributed to a supervisor, to peers, and to direct reports, all of whom rated how well we are doing. Do we “treat people with respect”? How well do we “coach others in the development of

their skills”? Literally hundreds of such questions. The ratings were anonymous, except for those submitted by a supervisor and those assigned to one’s self. Wary at first, most of us felt that it was a worthwhile exercise in self-assessment. In the end, it seemed a good idea to elicit the opinions of those who don’t often have an opportunity to make their voices heard. I know that I learned a lot about how my leadership style is perceived and what I can do to improve. We all did. Not sure I’m going to divulge all my strengths much less my weaknesses here, but I do want to thank everyone who pointed them out. ■

CARTOON

GRAÇA DORES



PreventionPOST

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