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French Trial Ended Due to Deaths Among Patients on Docetaxel-Doxorubicin Regimen

A breast cancer chemotherapy regimen that involved simultaneous administration of docetaxel and doxorubicin suppressed white blood cell activity in 40 percent of patients and led to two treatment-related deaths, concludes a report on the European RAPP-01 clinical trial published in the May 18 *Journal of the American Medical Association*.

The first death occurred in March 2000, when a 49-year-old patient became ill with abdominal pain 7 days after receiving the doxorubicin-plus-docetaxel regimen under study. She developed febrile neutropenia 2 days later and subsequently died. An autopsy was not performed, and the steering committee concluded that the death was "not specifically attributable" to docetaxel and decided to continue the trial. In January 2001, a second woman developed febrile neutropenia. She went into septic shock 6 days after her fourth cycle of doxorubicin and docetaxel but later recovered. In January 2003, a 39-year-old woman fell ill 6 days after first receiving the regimen. She died a week later from septic shock. The investigators ended the trial and switched the remaining patients in the docetaxel arm to the standard regimen of doxorubicin and cyclophosphamide.

Investigators have long known that combining docetaxel with doxorubicin can drop white cell counts, according to Dr. Jennifer Low, a senior investigator in the NCI's Cancer Therapy

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Director's Update

Advocates: Helping to Forge a Path to 2015

We use the term "cancer community" because, perhaps unlike any other disease area, there is a vast collection of groups and individuals who play an essential role in the cancer research enterprise.

In my time as director of the National Cancer Institute (NCI), I've come to more fully appreciate the complexity, robustness, and diversity of this collective, especially with regard to the advocacy community and its remarkable success in advancing cancer research.

The cancer advocacy community is rife with people who… take action to help others.

Just last week, for example, I participated in an event celebrating the 10th anniversary of the National Breast Cancer Coalition's Project LEAD. This program has helped to educate breast cancer advocates about the science of breast cancer, allowing them to work more closely with the research community in promoting new approaches to prevention, diagnosis, and treatment.

NCI recognizes the extensive reach

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Evaluation Program. Hence, the report underscores the importance of providing prophylaxis. "Febrile neutropenia is a serious risk with any doxorubicin-docetaxel regimen," said Dr. Low. "Prophylaxis—especially the use of growth factors—is used in all of the current trials with this regimen to help prevent febrile neutropenia and reduce the risk of septic death."

Because the trial was terminated early, the investigators were unable to determine if the docetaxel regimen extended survival. "At this time the doxorubicin-docetaxel regimen should not be recommended outside of carefully designed clinical trials," write the authors, who hail from several French research institutions including the Centre Rene Huguenin, Centre Leon Berard, and the Sainte Catherine Institute Breast Clinic.

While the docetaxel regimen caused less nausea and vomiting than the standard therapy, it was responsible for 72 of the 87 severe adverse events (82.8 percent) reported to the French Medicines Agency. Most of these events (87.5 percent) were related to febrile neutropenia.

One hundred twenty-six of 311 women (40.5 percent) receiving doxorubicin-docetaxel developed neutropenia accompanied by fever. In contrast, only 22 of 316 women (7 percent) taking the standard doxorubicin-cylcophosphamide therapy developed febrile neutropenia. The rates of neutropenia in the docetaxel arm were so high because, unlike similar studies conducted in the United States, the French trial did not employ prophylaxis for neutropenia. Patients received granulocyte-colony stimulating factor (G-CSF) only after their white cell count had already dropped.

Studies of doxorubicin-docetaxel combinations that employ prophylactic antibiotics or G-CSF report substantially lower rates of febrile neutropenia, according to Dr. Low. The Breast Cancer International Research Group 001 trial documented neutropenia in 24 percent of patients who received docetaxel, while the corresponding figure for the National Surgical Adjuvant Breast and Bowel Project B-27 trial was 21 percent.

Because the major risk from neutropenia is blood-borne infection, the antibiotic ciprofloxacin is sometimes given prophylactically to patients receiving docetaxel. But, said Dr. Low, "Most physicians now prefer using hematopoeitic colony-stimulating factors" because it boosts white cell production and is more effective than antibiotics. ◆

(Director's Upate continued from page 1)
and influence of the advocacy community—as advisors, educators, fund raisers, and legislative activists. NCI's Office of Liaison Activities (OLA) coordinates several programs that provide cancer research advocates with meaningful opportunities to offer guidance and feedback on NCI's priorities and initiatives.

Through the Consumer Advocates in Research and Related Activities (CARRA) program, for example, individual advocates can participate in the routine but important work that underlies much of what we do at NCI. Because of their expertise in patient issues, for instance, individual CARRA members are often asked to participate in the peer-review process, providing a consumer's perspective on research proposals.

The Director's Consumer Liaison Group (DCLG) gives the advocacy community a direct conduit to the NCI Director's office. DCLG, NCI's only all-consumer advisory group, played an important role in the launch earlier this year of a pilot initiative, the NCI "Listens and Learns" Web site. In its short existence, this Web site—http://ncilistens.cancer.gov/—has provided an important venue for cancer advocates to voice their opinions on some of the most pressing issues facing NCI.

OLA also coordinates teleconferences with advocacy groups to help them better understand and educate their constituencies about important new issues. Several months ago, for example, OLA coordinated a trans-HHS teleconference to clarify changes in Medicare reimbursement policies for cancer care. We plan to conduct a formal series of such educational teleconferences.

NCI also is engaged in a diverse array of initiatives with individual advocacy groups. Last year, the institute joined with the Pancreatic Cancer Action Network to launch an initiative that will create a map pinpointing researchers and clinical trials focused on pancreatic cancer. The goal is to facilitate the development of national strategies to maximize and leverage resources in the fight against pancreatic cancer.

The Lance Armstrong Foundation announced last week that it has sold more than 47.5 million of its yellow "Live Strong" bracelets. This demonstrates what can be accomplished by committed advocates with a good idea. The cancer advocacy community is rife with people who have been affected by cancer in one way or another and decided to take action to help others. I welcome their participation in the effort to achieve the 2015 goal, and I continue to be awed by the willingness and motivation that cancer advocates display every day. ◆

Dr. Andrew C. von Eschenbach
Director, National Cancer Institute

Cancer Research Highlights

Rituximab's Value Shown in First-Line Treatment of Follicular Lymphoma

The monoclonal antibody rituximab (Rituxan), when added to standard chemotherapy as a first-line treatment for follicular lymphoma, significantly delayed the progression of the disease and produced higher response rates, according to findings reported at the American Society of Clinical Oncology (ASCO) annual meeting last week by Dr. Kevin Imrie of the Toronto-Sunnybrook Regional Cancer Center in Canada.

Early results of the trial appeared in *Blood* in February, but the more extensive analysis Dr. Imrie reported provides "the first hard evidence that rituximab's demonstrated efficacy with recurrent disease" in follicular and other types of lymphoma extends to first-line treatment.

Previously untreated patients with advanced follicular lymphoma were randomly assigned: 162 patients received rituximab plus a standard first-line chemotherapy regimen of cyclophosphamide, vincristine, and prednisone (CVP); another 159 patients received CVP alone. After four cycles, only those patients who had responded remained in the study and received the final four cycles of whichever regimen they had begun.

Significant differences were seen for nearly all measures in favor of the rituximab-plus-CVP arm. About 81 percent of patients responded to rituximab therapy compared with 57 percent of patients in the CVP-only group. The rituximab patients had a longer median time before their cancer stopped responding to treatment (27 months vs. 7 months) and a longer median time during which their cancer continued to respond to treatment (35 months vs. 14 months). Side effects incidence was similar for both groups.

ADD Drug Shows Effectiveness Against "Chemobrain"

Researchers at the ASCO annual meeting last week reported that the use of a central nervous system stimulant significantly moderated cognitive dysfunction in patients previously treated with adjuvant chemotherapy. The data come from a phase III clinical trial testing the drug dexmethylphenidate, or d-MPH (Focalin)—a drug approved by the FDA for the treatment of attention deficit disorders—in patients with cognitive dysfunction following chemotherapy, a condition sometimes referred to as "chemobrain."

The study randomized 152 adult patients to treatment with d-MPH or to a control group. All patients had completed at least four cycles of chemotherapy for a variety of cancers. The vast majority of patients, 94 percent, were women with either breast or ovarian cancer. Only 132 patients completed the 8-week study, with the majority of dropouts related to adverse events, such as headache and nausea.

The treatment group showed weekly improvements in alertness and general cognitive function as measured by standardized assessment tools used in clinical trials, reported the study's lead author, Dr. Elyse Lower of the University of Cincinnati. Although the study was not designed to assess memory dysfunction, the treatment group showed significant improvement. But some of the overall assessment tools, she cautioned, did not show a statistically significant difference between test groups.

Laparoscopic Surgery for Colon Cancer Found Safe and Effective

Laparoscopic-assisted surgery for colon cancer is as effective as open surgery in the short term and is likely to produce similar long-term outcomes, according to a study reported in the May 14 *Lancet*.

Dr. Pierre J. Guillou and colleagues at the Medical Research Council (MRC) in the United Kingdom conducted a multicenter, randomized trial (dubbed CLASICC) of 737 colorectal patients during 1996–2002, comparing the standard open surgery with laparoscopic-assisted operations. About two-thirds of the patients were randomized to the laparoscopic treatment.

"Pathological analyses indicated high-quality surgery in both treatment groups, with high lymph-node yield equaling or exceeding that in several other trials," the researchers reported. "Our short-term results lend support to those of previous studies, which show that for colon cancer, the laparoscopic procedure is oncologically safe, that local recurrence rates will be no higher than for open surgery, and that cancer-related survival will be at least no lower than after conventional resection."

In an accompanying editorial, Stanford University professor Dr. Myriam Curet said this finding is reassuring for surgeons who have been concerned about earlier, smaller studies reporting

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Spotlight

Gene Discoveries Driving New Treatments for Kidney Cancer

It was 12 years ago that Drs. Marston Linehan, Berton Zbar, and colleagues from NCI's Center for Cancer Research (CCR) and elsewhere published a wonderful discovery. For many years they had studied families with Von Hippel-Lindau (VHL) syndrome, a rare, hereditary disease associated with benign tumors in multiple organs, but also with a form of the most common type of kidney cancer: clear cell renal cell carcinoma (RCC). The work paid off. They had linked VHL to a single gene on chromosome 3—the first gene found to cause kidney cancer. Research done since that time has shown that 60 to 80 percent of patients with nonhereditary, or sporadic, RCC have a VHL mutation.

Drs. Linehan, Zbar, and their NCI colleagues have led the search for additional genes associated with other forms of kidney cancer, an effort that has taken on increasing importance "because of the steady, relentless increase in its incidence since the early 1970s," Dr. Linehan says.

More than 36,000 patients are now diagnosed with kidney cancer every year. Although patients diagnosed with early stage disease have a 95 percent 10-year survival, in advanced disease, the odds of surviving for 2 years are less than 1 in 5. The current treatments for advanced disease are interferon α and interleukin 2 (IL-2). Although IL-2-based therapy can result in complete responses and may be effective in up to 20 percent of patients, it takes specialized expertise to administer and can be accompanied by serious side effects.

Since the VHL gene discovery, the researchers have discovered two other kidney cancer genes (see table), all via studies of families with hereditary forms of kidney cancer conducted at the NIH Clinical Center.

Of these genes, VHL has been the most intensively studied. In particular, researchers have been able to map some of the intracellular signaling pathways affected by this gene. Part of VHL's function is to help suppress tumor growth. But when a mutation arises in VHL that either silences it or greatly decreases its activity, it can have a serious domino effect, explains Dr. William G. Kaelin, a leading expert on the molecular biology of kidney cancer at Dana-Farber Cancer Institute. First, there is an overproduction of a transcription factor called HIF. This, in turn, spurs the production of growth factors such as VEGF and PDGF, both of which fuel cancer cell growth.

So the discovery of these genes, says Dr. Ronald M. Bukowski, director of the Experimental Therapeutics Program at the Cleveland Clinic Taussig Cancer Center, has been significant because it has allowed kidney cancer researchers to more rationally investigate agents "that might affect the pathways these genes modulate."

Over the last few years, in fact, a number of early-phase clinical trials testing a variety of targeted agents against advanced kidney cancer have generated much excitement. Earlier this month at the ASCO annual meeting, for example, researchers from the University of California, San Francisco reported on the results of a 52-patient, phase II trial testing AG-013736, an experimental agent that targets VEGF and PDGF. At 1-year follow-up, the drug prevented disease progression in three-quarters of the patients.

Hopeful results also have been reported with the experimental agents SU011248 and sorafenib, as well as with targeted drugs approved by the Food and Drug Administration for the treatment of other cancers such as bevacizumab (Avastin), which targets VEGF, and erlotinib (Tarceva), which targets EGFR, also in the VHL pathway.

These findings have significantly changed the perception of kidney cancer, says Dr. Kaelin. "Kidney cancer was one of those solid tumors that medical oncologists always thought were pretty intractable in terms of chemotherapy," he notes. "So it's ironic that…there is now a lot of excitement about using targeted agents against it."

Dr. Bukowski argues that more than just the perception of this disease has changed. The findings from these trials are demonstrating "a changed paradigm for the treatment of [advanced kidney cancer]," he says. "Whenever

Gene	Year	Kidney cancer type
VHL	1993	Clear cell renal cell carcinoma
c-Met	1997	Hereditary papillary renal carcinoma
BHD	2002	Chromophobe renal carcinoma

you change how you approach the treatment of a disease, that's big news. That's clearly something that's happening with this illness."

Dr. Linehan's laboratory recently launched a phase II clinical trial of an antibiotic derivative called 17AAG for the treatment of kidney tumors in patients with VHL disease. Dr. Len Neckers, a principal investigator in the Urologic Oncology Branch, worked with NCI's Developmental Therapeutics Program and Cancer Therapy Evaluation Program to translate 17AAG to the clinic. This agent blocks a so-called molecular chaperone that protects HIF—and other critical signaling proteins—from damage when tissues are under the stress of low oxygen. In laboratory and animal models, 17AAG has shown impressive antitumor activity.

Over the more than 2 decades of conducting this research, Dr. Linehan recounts, the progress has been slow but steady.

"You can cure tumors in animals, you can cure them in the lab," he says. "We just have to go one step at a time. We're in this for the long haul, and I have hope that we'll get there." ◆

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higher rates of recurrence of colorectal cancer after laparoscopic operations.

However, for patients undergoing anterior resections for rectal cancer, MRC researchers found that a "nonsignificant difference in CRM (circumferential resection margin) positivity was recorded, suggesting that the laparoscopic procedure could be associated with a slightly raised risk of local recurrence." The researchers did not recommend routine use of the less-invasive procedure in those cases. ◆

A Conversation with Drs. Marston Linehan and Berton Zbar

Drs. Linehan and Zbar have worked together for more than two decades on determining the molecular basis of kidney cancer in order to provide the foundation for finding more effective treatments. They talked with the NCI Cancer Bulletin *about where they have been and where this research is headed.*

Can you talk about the role of studying families in your work over the years?

Dr. Linehan: In the mid-1980s, we showed loss of chromosome 3 in patients with sporadic kidney cancer, and we published a paper in *Nature* saying that this could indicate there is a cancer gene in this location. But it was just going to take too long to find the gene at the rate we were going. Dr. Al Knudson, who pioneered the study of genetics in cancer, suggested that looking at families with hereditary forms of kidney cancer would help us identify the gene.

Dr. Zbar: We sent letters to physicians in the United States and Canada to recruit families with hereditary renal carcinoma. Physicians were targeted based on the specific clinical characteristics of the disease under study. I worked with a small NCI team to evaluate renal carcinoma families, which included conducting detailed medical histories and collecting blood samples for DNA analysis at our laboratory at NCI-Frederick.

We then set up a large, multidisciplinary team to evaluate patients. We constructed family trees and performed genetic mapping, then physical mapping in the hope of finding the disease genes. We've seen families from all over this country and, really, all over the world.

After everything that's been accomplished, is it now just a matter of seeing which agents are most effective in clinical trials?

Dr. Linehan: I'm not naïve about the tenacity of these tumors. As a clinician who has managed patients with metastatic disease, I believe that by studying the pathways and testing the agents that block those pathways, we have a very good plan for progress.

Dr. Zbar: It would be extremely useful to identify molecular markers to determine which patients will be the best candidates for the various targeted treatments. The presence (or absence) and specific type of somatic VHL mutation would be one genetic alteration that might predict response of metastatic renal carcinomas to drug therapy. ◆

Funding Opportunities

Following are newly released NCI research funding opportunities:

Global Network for Women's and Children's Health Research

RFA-HD-05-025
Letter of Intent Receipt Date: Dec. 19, 2005
Application Receipt Date: Jan. 19, 2006

This is a renewal of RFA-HD-00-007 and RFA-HD-01-024. This funding opportunity will use the Cooperative Research Project Grant (U01) award mechanism. For more information see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=2704. Inquiries: Dr. Linda L. Wright—wrightl@mail.nih.gov.

Pilot and Feasibility Program Related to the Kidney

PA-05-103
Application Receipt Dates: Sept. 10, 2005; Jan. 10, May 10, and Sept. 10, 2006; Jan. 10, May 10, and Sept. 10, 2007; Jan. 10 and May 10, 2008

This funding opportunity will use the NIH Exploratory/Development Research Grant (R21) award mechanism. For more information see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=2706. Inquiries: Dr. Judy Mietz—jm166o@mail.nih.gov.

Functional Links Between the Immune System, Brain Function, and Behavior

PA-05-054
Application Receipt Dates: Sept. 10, 2005; Jan. 10, May 10, Sept. 10, 2006; Jan. 10, May 10, Sept. 10, 2007; Jan. 10 and May 10, 2008

This PA will use the NIH research project grant (R01), Small Grant (R03), and Exploratory/Developmental grant (R21) award mechanisms. For more information see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=2744. Inquiries: Dr. Paige McDonald—mcdonalp@mail.nih.gov. ◆

Featured Clinical Trial

Ginger Treatment For Cancer-Related Nausea and Vomiting

Name of the Trial

Phase II Randomized Study of Ginger in Patients with Cancer and Chemotherapy-Induced Nausea and Vomiting (CCUM-0201). See the protocol summary at http://cancer.gov/clinicaltrials/CCUM-0201.

Dr. Suzanna Zick, Principal Investigator

Principal Investigator

Dr. Suzanna Zick, University of Michigan Integrative Medicine.

Why Is This Trial Important?

Nausea and vomiting are among the most distressing and feared side effects of cancer and cancer treatment. Beyond being unpleasant, the nausea and vomiting associated with cancer and its treatment can lead to serious and life-threatening complications, such as nutritional depletion, metabolic imbalance, esophageal damage, expulsion of oral chemotherapy agents, and withdrawal from potentially curative treatment. Thus, effective treatment for nausea and vomiting is critical to the care of cancer patients.

In this trial, researchers are testing the ability of two different doses (lower vs. higher) of the herb ginger to treat delayed nausea and vomiting associated with chemotherapy. Ginger is believed to affect receptors in the digestive tract for the neurotransmitter serotonin. This action is similar to conventional antinausea drugs.

"Ginger has been shown to be effective in a number of clinical trials against nausea and vomiting associated with motion sickness, pregnancy, and postoperative recovery," said Dr. Zick. "With this trial, we hope to determine its efficacy and safety for chemotherapy-induced nausea and vomiting.

"We hope ginger will be effective for patients who continue to experience delayed nausea and vomiting despite treatment with other antinausea drugs," Dr. Zick added.

Who Can Join This Trial?

Researchers seek to enroll 180 cancer patients aged 18 or older who are undergoing chemotherapy and have experienced nausea or vomiting during or following a previous treatment cycle. See the full list of eligibility criteria at http://cancer.gov/clinicaltrials/CCUM-0201.

Where Is This Trial Taking Place?

The study is being conducted at sites in the United States through the Community Clinical Oncology Program (CCOP) and elsewhere. See the list of study sites at http://cancer.gov/clinicaltrials/CCUM-0201.

Contact Information

For more information, see the list of study contacts at http://cancer.gov/clinicaltrials/CCUM-0201 or call the NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237). This call is completely confidential. ◆

An archive of "Featured Clinical Trial" columns is available at http://cancer.gov/clinicaltrials/ft-all-featured-trials.

Notes

Ihde Memorial Lecture Slated for June 3

The first annual Daniel C. Ihde Memorial Lecture will take place on June 3 at 12:00 p.m. in the Clark Auditorium at the National Naval Medical Center in Bethesda, Md.

Dr. Daniel C. Ihde

Dr. John Minna, director of the Hamon Center for Therapeutic Oncology Research at the University of Texas Southwestern Medical Center, will discuss "Molecular Pathogenesis of Lung Cancer with Translation to the Clinic."

Dr. Ihde's career at NCI spanned 21 years; he served as NCI deputy director from 1991–1994. He died on Dec. 9, 2004. Dr. Minna, past chief of the NCI/Navy Medical Oncology Branch, worked with Dr. Ihde to bring the NCI branch to the National Naval Medical Center in 1981. For more information about the lecture, contact Joyce Stocker at 301-435-5399.

Nanotechnology Report Cites NCI Plan

On May 18, the President's Council of Advisors on Science and Technology (PCAST) released the report, "The National Nanotechnology Initiative at Five Years: Assessment and Recommendations of the National Nanotechnology Advisory Panel." The report is PCAST's first assessment of the federal government's nanotechnology research efforts.

The report cites NCI's Cancer Nanotechnology Plan as a good example of an individual federal agency identifying performance-based targets for its nanotechnology funding initiatives. The report also cited the development of quantum dots as imaging agents for metastases as an example of nanotechnology being applied in a novel manner to solve a pressing medical need.

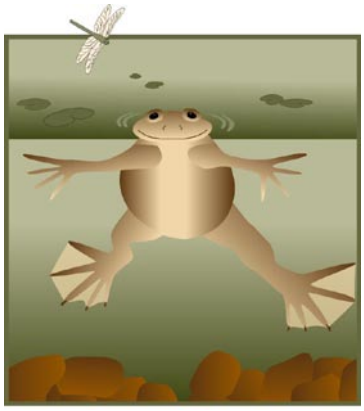
To view the full report, go to www.ostp.gov/pcast/pcast.html.

EDRN Awards Grants

On May 12, NCI's Early Detection Research Network (EDRN) awarded 13 grants totaling $11 million to complete funding for the next 5 years of research. EDRN brings together dozens of institutions to help accelerate the translation of biomarker information into clinical application and to evaluate new ways of testing for cancer risk and cancer in its earliest stages. Grants were awarded to eight clinical epidemiology and validation centers, which conduct the early phases of clinical and epidemiological research on the application of biomarkers; four biomarker reference laboratories, which work to validate the biomarker tests; and one data management and coordinating center/informatics center, which provides logistical, informatics, and statistical development and support.

Spring Research Festival at NCI-Frederick

The ninth annual NCI-Frederick/Ft. Detrick Spring Research Festival took place on May 18 and 19 at the NCI at Frederick Campus. The festival is held each spring as a forum for scientists from the agencies represented at Fort Detrick: NCI's CCR, the National Institute of Allergy and Infectious Diseases, the U.S. Department of Agriculture, the Army Medical Research and Materiel Command, and the Department of Homeland Security. This year's festival showcased displays of individual researchers' work, local nonprofit organizations, and new biomedical equipment and supplies. The festival's keynote address was delivered by Nobel laureate J. Michael Bishop, Chancellor of the University of California, San Francisco, who spoke on the use of mouse models in human cancer research. The festival also sponsored a screening and discussion of the 1987 film, *The Race for the Double Helix*, as part of the NCI-Frederick Scientific Library's "Science in the Cinema" program. The film dramatized the work of scientists Watson, Crick, and others as they worked to unravel the structure of DNA; the screening was followed by a discussion led by Dr. Mary Carrington, a principal investigator at NCI-Frederick.



Each year the festival selects a mascot whose properties have shown potential for fighting or preventing disease. This year's emblem was Claude the African Clawed Frog, or *Xenopus laevis*. Originally found only in Africa, these frogs have achieved scientific notoriety through their production of magainin, a substance found on their skin that has, among other properties, anticancer, anti-inflammatory, angiogenic, and wound-healing properties.

For additional information on the festival, go to http://web.ncifcrf.gov/events/springfest/geninfo.asp. ◆

Community Update

Cancer Risk Prediction Models: Priorities for Future Research

More than 100 researchers met last May at an NCI-sponsored workshop on statistical models for predicting a person's risk of developing cancer. A detailed report on the meeting, including recommendations for future research on cancer risk prediction models, appears in a commentary in the May 18 *Journal of the National Cancer Institute*.

Participants identified research priorities and resources in the areas of: 1) revising existing breast cancer risk assessment models and developing new models; 2) encouraging the development of new risk models; 3) obtaining data to develop more accurate risk models; 4) supporting validation mechanisms and resources; 5) strengthening model development efforts and encouraging coordination; and 6) promoting effective cancer risk communication and decision-making.

The workshop included epidemiologists, statisticians, geneticists, clinicians, and genetic counselors, among others. They identified strengths and limitations of cancer and genetic susceptibility prediction models in use or under development, and they explored methodological issues related to their development, evaluation, and validation.

"This meeting brought together a diverse group of scientists to talk about how we can develop and improve our current statistical tools for predicting the development of cancer," says Dr. Andrew Freedman of NCI's Division of Cancer Control and Population Sciences, who co-chaired the meeting.

"There's been a lot of interest in cancer risk prediction models, and now is an important time to explore issues involved in developing, applying, and evaluating these models," says Dr. Freedman.

The workshop focused attention on risk prediction models and "actually has spurred quite a bit of research activity" since last spring, notes Dr. Ruth Pfeiffer of NCI's Division of Cancer Epidemiology and Genetics, (DCEG), the other co-chair. DCEG staff are working on models for melanoma and colorectal cancer, and criteria for evaluating risk models.

Among the findings to emerge from the workshop, Dr. Pfeiffer says, is the importance of communication between the people who develop the models and the people who use them.

The number of risk models has grown steadily since a model for predicting the risk of heart disease was published in 1976. In the late 1980s, researchers began to publish models that predicted a woman's risk of breast cancer based on such risk factors as age, age at menarche, age at first live birth, and family history of the disease.

Today, statistical models are widely used by physicians to make decisions about cancer prevention and treatment. Like clinicians and researchers, the public is interested in cancer risk prediction, as is clear from the number of related Web sites, handbooks, and information resources from professional societies.

A number of companies in the United States and the United Kingdom offer genetic risk profiling. "With the proliferation of new risk models, there's been a concern that the models are used appropriately, and this was one reason for the workshop," notes Dr. Freedman. ◆

Featured Meetings and Events

A comprehensive calendar of cancer-related scientific meetings and events sponsored by NCI and other scientific organizations is available at http://calendar.cancer.gov. ◆

The *NCI Cancer Bulletin* is produced by the National Cancer Institute (NCI). NCI, which was established in 1937, leads the national effort to eliminate the suffering and death due to cancer. Through basic, clinical, and population-based biomedical research and training, NCI conducts and supports research that will lead to a future in which we can identify the environmental and genetic causes of cancer, prevent cancer before it starts, identify cancers that do develop at the earliest stage, eliminate cancers through innovative treatment interventions, and biologically control those cancers that we cannot eliminate so they become manageable, chronic diseases.

For more information on cancer, call 1-800-4-CANCER or visit http://www.cancer.gov.

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