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NCI Cancer Bulletin

Eliminating the Suffering and Death Due to Cancer

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Twist Protein Significant Contributor to Breast Cancer Metastasis, Study Finds

Breast cancer tumor cells' ability to travel through the body and form distant tumors appears to rely on their ability to appropriate a "sleeper protein" that plays an important role in early embryonic development, according to a study published in the June 25 *Cell*.

The protein, known as Twist, regulates genes and is critical to cellular communication and cell allocation into various tissues during embryonic development. Twist typically remains dormant after embryo development is complete. However, in a study by a research team from the Whitehead Institute, led by Dr. Robert Weinberg, breast cancer tumor cells were shown to reactivate the protein. Thanks to this molecular hijacking, "cancer cells acquire in one fell swoop many of the abilities they need to execute the complex stages of metastasis," said Dr. Weinberg.

The study, funded in part by the National Cancer Institute (NCI), involved both a mouse model and tissue samples of human breast cancers, with each step in the investigation implicating Twist

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Director's Update

Measuring Our Progress on Prostate Cancer

Prostate cancer is an ideal example of the successes, challenges, and setbacks we have experienced in our efforts to eradicate cancer. Prostate cancer remains the most common cancer overall and the second leading cause of cancer-related death in men. And, unfortunately, African American men continue to be disproportionately affected by prostate cancer to a significant degree.

Nevertheless, it's estimated that there are approximately 1.7 million prostate cancer survivors in the United States today and prostate cancer mortality has decreased by 4 percent per year since 1994—evidence that we are indeed making progress against this particular foe.

Last week, I spoke at the annual meeting of the Canadian Urological Association and talked with attendees about the headway that has been made on prostate cancer, including some of the findings from the

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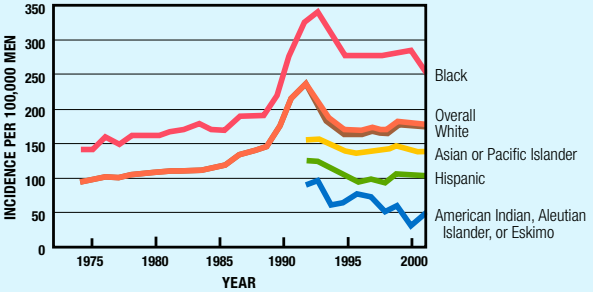
Prostate Cancer Incidence



Rates are per 100,000 and age-adjusted to the 2000 U.S. standard; Confidence intervals are 95% for rates.

(Twist Protein continued from page 1)
as a critical component of metastasis. The gene that encodes for Twist, the team found, was highly expressed in metastatic mouse tumor cell lines but not in nonmetastatic lines. To prove this point, metastatic mouse tumor cells devoid of Twist were injected into the mammary pads of mice. The result: Primary tumors formed but were unable to metastasize.

In addition, cultures of blood samples from mice showed that Twist aids tumor cells' efforts to slip into the blood stream; other components of the study may show how. In tests on normal mammalian cells, the introduction of cells that express Twist promoted an epithelial-mesenchymal transition (EMT), a molecular event that results in a cellular conversion, causing bound epithelial cells to lose the protein E-cadherin, separate from each other, alter their shape, and acquire the proteins needed for motility and invasion.

Finally, based on the results of the earlier tests, team members from Brigham and Women's Hospital reanalyzed data on 57 tumor samples from 3 aggressive human breast cancer subtypes. Of the 3, Twist was expressed in 70 percent of invasive lobular carcinomas—a subtype characterized by almost complete E-cadherin depletion.

"We were seeing the same phenotype and gene expression correlation in human breast tumors," said paper co-author Dr. Andrea Richardson, a pathologist at Brigham and Women's Hospital.

A number of previous studies have shown that loss of E-cadherin expression occurs in many carcinomas "which was correlated with a more invasive and metastatic phenotype," said study lead author Dr. Jing Yang. "Therefore, we think that suppression of E-cadherin by Twist could be an important function" in cancer metastasis.

Dr. Suresh Mohla, chief of the Tumor Biology and Metastasis Branch in NCI's Division of Cancer Biology, concurs. "Together, the findings present a good picture that the activation of Twist and Twist-induced EMT are important components for tumor metastasis," he said.

"There are many barriers in metastasis, and it is considered a very inefficient process," Dr. Mohla continued. "A normal tumor may shed millions of cells a day, but very few survive. These investigators showed that tumor cells are very clever and are able to overcome these barriers by appropriating a very latent protein that helps them move in and out of blood and into tissues, form new colonies, and grow."

Other studies have pointed to genes that are important components of metastasis in other cancers, Dr. Mohla explained, including a recent one that implicated Rho-C in metastatic melanoma.

As for Twist, while research into how it functions in metastasis is still preliminary, Dr. Yang said the available evidence does point to potential diagnostic and treatment applications. ◆

(Director's Update continued from page 1)
Prostate Cancer Progress Report, recently posted on cancer.gov at http://prg.cancer.gov/prostate/progress.pdf. The report provides a comprehensive overview of NCI's efforts from 1998 to 2002 in response to the Progress Review Group (PRG) recommendations on prostate cancer issued in 1998—the first-ever NCI PRG report.

During those 5 years, NCI tripled funding for prostate cancer research, from $86.9 million to $278.4 million, nearly doubled the number of projects relevant to prostate cancer, more than doubled the relevant individual training and career development awards, and expanded the prostate Specialized Programs of Research Excellence network from 3 to 11 sites.

As the *Progress Report* documents, we now better understand this disease and how to prevent and treat it. NCI-supported research published in 2001 and 2002, for example, has shown that the protein TGF-beta plays an important role in initiating and promoting angiogenesis and prostate tumor growth. In one experimental model, use of a TGF-beta inhibitor resulted in prostate tumors that had fewer blood vessels and were half the size of tumors in the control group. Meanwhile, because of survival improvements seen in an NCI-sponsored clinical trial, early initiation of hormonal therapy is now the standard of care in node-positive prostate cancer patients. And in the area of prevention, the NCI-sponsored Prostate Cancer Prevention Trial (PCPT), published in 2003, found that the drug finasteride reduced prostate cancer incidence by 25 percent. The study provided a cautionary note, however, as finasteride use also was associated with higher grade tumors.

NCI researchers are continuing to mine blood and tissue samples and data collected during PCPT. As reported last month in the *NCI Cancer Bulletin*, in a study published in the *New England Journal of Medicine*, NCI researchers analyzed biopsy samples from almost 3,000 men in the PCPT placebo arm and found that up to 15 percent of men with prostate-specific antigen (PSA) levels below 4 nanograms/milliliter and normal digital rectal exams have prostate cancer and that 15 percent of these cancers are high-grade.

These data highlight the need to develop prognostic markers beyond
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Cancer Research Highlights

Docetaxel-Thalidomide Combo Increases Survival Rate in Prostate Cancer Patients

Survival rates increased and prostate-specific antigen (PSA) levels decreased in men with androgen-independent prostate cancer (AIPC) when they were treated with thalidomide in addition to docetaxel, compared with docetaxel alone, according to a study by Dr. William Dahut and his colleagues at NCI's Center for Cancer Research, reported in the July 1 *Journal of Clinical Oncology*.

In a randomized phase II trial of 75 men with chemotherapy-naive metastatic AIPC, patients received either docetaxel alone or combined with thalidomide. Docetaxel has been shown to decrease PSA levels in AIPC patients. After a 26.4-month follow-up, the combination group had a 53 percent PSA decline compared with a 37 percent decline in the docetaxel-only group. The combination group also had a median progression-free survival of 5.9 months compared with 3.7 months in the monotherapy group. At 18 months, the combination group had an overall survival rate of 68.2 percent compared with 42.9 percent with docetaxel alone.

According to the researchers, the study represents the first randomized trial suggesting that an anti-angiogenesis agent may be helpful in treating prostate cancer. "Combination therapy with a chemotherapeutic agent and an angiogenesis inhibitor represents a promising new area of investigation for metastatic AIPC," said Dr. Dahut, "But the small numbers of patients in this study means that statistical significance has not been reached, and larger randomized trials are needed."

Nitric Oxide Amount and Duration Affect Key Tumor-Related Proteins

Certain key proteins involved in tumor development have been found to respond to the concentration and duration of nitric oxide (NO). According to a study in the June 15 issue of the *Proceedings of the National Academy of Sciences*, Dr. Douglas Thomas of the Radiation Biology Branch in NCI's Center for Cancer Research and his colleagues found that the dose and duration of NO exposure had a significant effect on the regulation of three proteins—hypoxic inducible factor 1α (HIF-1α), extracellular signal-regulated kinase (ERK), and p53 in MCF7 breast cancer cells.

Of almost 20 proteins surveyed, only ERK, HIF-1α, and p53 responded differentially to NO levels—ERK to low NO concentrations, HIF-1α to medium, and p53 to the highest concentrations. They also noted that the duration of NO exposure affected these signal transduction responses. ERK was rapidly phosphorylated, but the effect was transient. HIF-1α accumulation continued only when there was an adequate, sustained NO flux. The response of p53 was detected during NO exposure and persisted for 12 hours afterwards.

While many studies have shown that NO is involved in a variety of physiological functions important to tumor survival, this is the first study to quantify the effects of NO dose and concentration on proteins critical to tumor development in a breast cancer cell line. In solid tumors, cell density and oxygen gradients will also regulate the response of proteins to NO.

"The role of NO as either growth-promoting or cytotoxic in tumors may be explained by differences in both the concentration and exposure time of cells to NO," Dr. Thomas reported. ◆

(Director's Update continued from page 2)

PSA and tumor grade to identify men most likely to benefit from treatment. And NCI is doing just that. The NCI Early Detection Research Network, for example, is working toward developing and validating genomic and proteomic technologies to identify biomarkers of prostate cancer prognosis. In addition, NCI researchers are conducting molecular epidemiological studies using samples collected during PCPT to identify men with genetic polymorphisms that make them most likely to benefit from prevention strategies that use finasteride.

Then there are trials like the NCI-funded SELECT, a study that has completed enrollment (with approximately 35,000 participants thus far) and should provide important information on whether the dietary supplements selenium and vitamin E can prevent prostate cancer.

There are, of course, critical gaps in our understanding of prostate cancer. But in many ways, this malignancy is representative of our overall effort against cancer. Progress has been incremental, and new insights often beget new questions. But there is a consistent flow of fresh ideas and intriguing findings that spurs us forward, driving the research engine that translates discoveries into real advances for patients. ◆

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

HHS News

Medicare Prescription Drug Coverage Pilot Includes Oral Cancer Drugs

Up to 50,000 Medicare patients will participate in a demonstration project that provides prescription drug coverage, including coverage of 12 oral anticancer drugs, U.S. Department of Health and Human Services Secretary Tommy Thompson announced on June 24. Under the Medicare Replacement Drug Demonstration program, Medicare will cover prescription drugs for several serious diseases and life-threatening conditions. The program will initially be open to 50,000 current Medicare beneficiaries. It will allow for the spending of $500 million on covered drugs, before the Medicare Prescription Drug, Improvement, and Modernization Act (MMA) comes into effect in 2006.

A full 40 percent of the total funding will be earmarked for oral cancer drugs that patients can take at home. The remaining 60 percent will be allocated for drugs for other debilitating conditions, such as multiple sclerosis and rheumatoid arthritis. In this preview of MMA, beneficiary co-payment and cost sharing will mirror what will be the standard Medicare Part D prescription drug benefit in 2006, but will operate without the monthly premium that will eventually be paid by patients.

Under the pilot, Medicare will cover 26 drugs, including prominent cancer therapies such as tamoxifen for breast cancer, imatinib (Gleevec) for chronic myelogenous leukemia and gastrointestinal stromal tumors, thalidomide for multiple myeloma, and gefitinib (Iressa) for lung cancer. A full list of the covered drugs is available at http://www.cms.hhs.gov/researchers/demos/MMAExternalQsAs_6_23_04.pdf.

"The potential to increase the availability of many of the new, orally active cancer therapies is likely to be of major benefit to a significant number of cancer patients who receive Medicare benefits," said Dr. James H. Doroshow, director of NCI's Division of Cancer Treatment and Diagnosis. Cost savings to beneficiaries could range from 75 to 90 percent, depending on the drug and financial situation of the participant.

To be eligible for the demonstration, beneficiaries

- Must be currently enrolled in Medicare Part A and Part B;
- Must indicate Medicare as their primary payer and may not have comprehensive drug coverage through other sources; and
- Must provide a signed certificate from a doctor that they require one of the drugs covered under the plan for an indicated disease.

Applications may be submitted from July 6 to Sept. 30, 2004, and can be downloaded at http://www.cms.hhs.gov/researchers/demos/drugcoveragedemo.asp. For more information, call 1-866-563-5386, TTY 1-866-563-5387. ◆

Special Report

Report to the Nation, Nanotech Proposal Presented to BSA

During the June meeting of NCI's Board of Scientific Advisors (BSA), members got a snapshot of the past and a glimpse of the future. Members heard an in-depth presentation on the recently released *Annual Report to the Nation on the Status of Cancer*, as well as a proposed strategic plan to develop and promote nanotechnology-based cancer research. Issues such as opportunities for cancer research in the NIH Roadmap initiative, legislative and congressional matters, grant payline and application trends, progress of the NCI clinical trials working group, and others were included on the agenda.

BSA's role is to provide scientific counsel related to NCI extramural programs. As part of its overall plan for the discovery, development, and delivery of advanced technologies, NCI presented a nanotechnology concept for review by BSA. The potential role of nanotechnology and nanoscience in accelerating progress in all areas of cancer diagnosis, treatment, and prevention was also highlighted in a presentation by Drs. Mauro Ferrari and Gregory Downing. The Board will meet on July 12 to finalize their review of this concept.

Report to the Nation: Proof of Progress

BSA members were enthusiastic about the *Report to the Nation* and, as reported in the June 8 *NCI Cancer Bulletin*, the finding that overall

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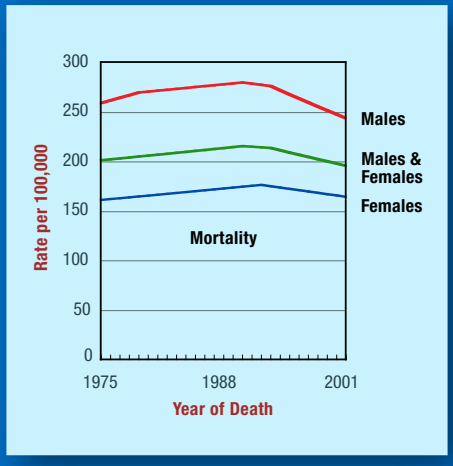
(Special Report continued from page 4)
cancer incidence and mortality have decreased. BSA members encouraged NCI to increase efforts to disseminate key elements of the annual report to nonscientific audiences. One member commented that the report's release provides an important "teachable moment" for the cancer community, representing an opportunity to highlight the progress that has been and continues to be made against cancer.

Board members were particularly excited about the recent decrease in lung cancer mortality among women. Lung cancer is still the leading cause of cancer deaths and true breakthroughs in treatment have been limited, cautions Dr. Brenda K. Edwards, a senior author of the *Report to the Nation*, who made the BSA presentation.

U.S. Death Trends, Cancer of All Sites, 1975–2001



- Decline of -1.1% per year since 1993
- Decline for men is -1.5% per year since 1993
- Decline for women is -0.8% per year since 1992
- Decline continues for Prostate, Breast (F), Colorectal, Lung (M), and many other sites
- Lung (F) is now stable

"Seeing the decline in lung cancer death rates for women is an important statement that we can have an impact on cancer, for example, through reductions in smoking," says Dr. Edwards, associate director of the Surveillance Research Program in NCI's Division of Cancer Control and Population Sciences. The findings, she adds, are the result of "changes in women's behavior that took place a long time ago, and efforts to prevent and control the use of tobacco must continue because it takes many years to see a benefit in cancer rates."

This year's *Report to the Nation* should again prove to be a useful tool for public health officials, researchers, and the advocacy community, Dr. Edwards notes. In addition to providing updates on the four most common cancers, this year's *Report* features information on less common cancers for five race and ethnic populations, as well as data on prognosis and survival associated with diagnosis at specific stages of disease. It also focused on another burgeoning area of interest and research: survivorship.

Viewed as a whole, the *Report to the Nation* provides an encouraging picture. "On balance," Dr. Edwards says, "when you look closely across all the specific cancer sites, the improvements in cancer rates and patient prognosis point to real advances in risk reduction, early detection, treatment, and medical management." ◆

A Conversation with Dr. Brenda Edwards

Dr. Brenda Edwards has been associate director of the Surveillance Research Program and its predecessor organizational unit in NCI's Division of Cancer Control and Population Sciences since 1989. She has been involved in cancer prevention and control since its formative days in the early 1980s. Dr. Edwards began her affiliation with NCI in 1978 as a researcher in cancer treatment clinical trials, and 4 years later joined the team conducting some of the first cancer prevention trials. Her research has included the full spectrum of cancer surveillance, including risk factors, patterns of care, behavioral studies and survivorship, statistical methodology, and analytic activities.

The *Report to the Nation* provides a wealth of information. What is different or notable about this year's report?

This year we gave a fair amount of attention to many types of cancers because it's important to bring attention to the full spectrum of cancer as it affects all people. We were also very intentional about
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providing substantial information about survival. That's what makes a resource like this so valuable, because the data can be used to describe the burden of cancer, the past successes, and the challenges for the future in a whole host of cancer sites for different population groups.

Survivorship is an area of intense focus. How did you handle that in the *Report*?

We knew that it's difficult to document progress via survival data, so we included all of the caveats. The increases in screening, for example, can actually alter the proportion of patients who have early-stage disease, which is going to improve the survival figure. Some people have argued that this skews the results. The data show that with effective screening and with improved treatments, over a long time ultimately you will lower the population mortality rates.

So a report like this really has many uses for the entire cancer community?

Yes. We've heard from many people that the *Report* often serves as a key resource document for their work. They know they can turn to it to bring them up to date on incidence, mortality, and, this year of course, there is a lot of survival data. It's a little easier to use than posting hundreds of pages on the Web. ◆

Featured Clinical Trial

Chemotherapy for Secondary Neoplastic Meningitis

Name of the Trial

Phase I Study of Intrathecal Gemcitabine in Patients with Neoplastic Meningitis Secondary to Leukemia, Lymphoma, or a Solid Tumor (NCI-03-C-0032). See the protocol summary at http://cancer.gov/clinicaltrials/NCI-03-C-0032.

Principal Investigator

Dr. Lisa Bomgaars, Texas Children's Cancer Center

Dr. Lisa Bomgaars
Principal Investigator

Why Is This Trial Important?

Neoplastic meningitis is a condition in which cancer cells spread into the membranes surrounding the brain and the spinal cord (the meninges). Often, the condition is associated with cancer that has spread from tumors elsewhere in the body. Neoplastic meningitis is difficult to treat because chemotherapy drugs injected intravenously often do not reach high enough concentrations in the meninges to be effective. Consequently, chemotherapy for neoplastic meningitis is often given intrathecally, injected into the fluid-filled space between the meninges.

This study seeks to determine whether the drug gemcitabine (Gemzar) may be effective in treating neoplastic meningitis caused by the spread of a primary leukemia, lymphoma, or solid tumor. Gemcitabine is active against many of types of cancer that tend to spread to the meninges, and may prove effective in treating secondary neoplastic meningitis.

"The agents available to treat neoplastic meningitis are quite limited," said Dr. Bomgaars. "Gemcitabine is an agent that works differently from other treatments for this condition. If effective, it will be a welcomed new option for patients fighting neoplastic meningitis."

Who Can Join This Trial?

Researchers seek to enroll 25-30 patients aged 3 and over who have been diagnosed with neoplastic meningitis secondary to an underlying leukemia/lymphoma or a solid tumor (including primary central nervous system tumors or carcinomas of unknown primary site) for which there is no conventional therapy. See the full list of eligibility criteria at http://cancer.gov/clinicaltrials/NCI-03-C-0032.

Where Is This Trial Taking Place?

Study sites in the United States are enrolling patients in the trial. See the list of sites at http://cancer.gov/clinicaltrials/NCI-03-C-0032.

Who To Contact

See the list of study contacts at http://cancer.gov/clinicaltrials/NCI-03-C-0032 or call the NCI's Clinical Studies Support Center (CSSC) at 1-888-NCI-1937. The call is toll free and completely confidential. ◆

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

Notes

Leischow Receives Award

Dr. Scott Leischow, acting associate director of NCI's Behavioral Research Program in the Division of Cancer Control and Population Sciences will receive an NIH Director's Award at a ceremony on July 22. Dr. Leischow's outstanding contributions to the NIH include highly effective communications while testifying to Congress, IC directors, HHS staff, and leaders of advocacy organizations on tobacco-related issues. His outstanding leadership on behalf of NCI, NIH, and HHS on research concerning tobacco use, prevention, and cessation are also recognized with this award.

NLST Finalizes Enrollment

The National Lung Screening Trial (NLST) has completed enrollment with 53,419 volunteers, more than 3,400 over its initial goal. The trial, which is comparing chest x-ray and spiral computer tomography (CT) to determine if one method is better than the other at reducing cancer deaths, had aimed to accrue 50,000 participants in 2 years. The first participants were enrolled in September 2002 and by January 2004, more than 6 months earlier than expected, 50,000 people had joined. The trial remained open to accrual after January only in sites that were either still screening participants for eligibility or participating in the archiving of blood, urine, and phlegm for studies of potential biomarkers or tumor markers. The 30+ NLST sites are now closed to recruitment.

Recruitment to the study was accomplished in partnership with the American Cancer Society, whose regional offices helped raise awareness of the trial in their communities. The study is funded by NCI and administered through the Division of Cancer Prevention via the Prostate, Lung, Colorectal and Ovarian Cancer Trial screening network and the Division of Cancer Treatment and Diagnosis through a grant to the American College of Radiology Imaging Network.

Dennis Recognized for Lung Cancer Research

Dr. Phillip Dennis of NCI's Cancer Therapeutics Branch has been awarded the 2004 Alton Ochsner Award for his research showing that activation of the PI3K/Akt signal transduction pathway may be an early and important event in lung cancer formation and therapeutic resistance. The award will be presented at the annual convocation of the American College of Chest Physicians on October 28 in Seattle. The award honors Dr. Alton Ochsner, one of the founders of the Ochsner Clinic Foundation and the first person to recognize that cigarette smoking is the primary cause of lung cancer.

Garcia Recognized for Outreach

Dr. Roland Garcia, program director of NCI's Disparities Research Branch, was presented with the National Healthcare Hero Award in recognition of his leadership and commitment to improving patient access to quality health care. He was particularly commended for his outreach to underserved populations, specifically Native American and Alaska Native populations, with the goal of reducing the disparities in access to care.

Dr. Garcia was an inaugural recipient of this annual award, which was presented at the Patient Advocate Foundation's Fifth Annual Patient Congress on June 24. The Patient Advocate Foundation is a national nonprofit organization that serves as a liaison between patients and their insurers, employers, and/or creditors to resolve financial and other matters related to their diagnosis.

Flat NCI Budget Results in Funding of Fewer Competing New Training Grants

Although both the NCI allocation for training and the total number of funded training awards increased in 2004, the number of competing awards funded was significantly lower than in recent years. This paradoxical situation stems from NCI's ongoing commitments to existing continuing grants. Over the past 5 years while NCI's budget increased, the number of training awards also increased sharply. For FY 2004, funds available for new competing grants came from the completion of grants funded 5 years ago. The number of grants that ended was small in relation to the number of applications. To mitigate the impact of this effect, NCI allocated an additional $4 million for new awards.

Despite this increased allocation, fewer new and competing training awards will be made this year than in the previous 4 years. NCI will fund 71 K grants in 2004, including 23 awards to minority investigators, (compared with 124 in 2003), and 12 R25 grants (compared with 24 in 2003). In contrast, National Research Service Award grants did reasonably well. NCI anticipates similar difficulties in 2005, depending on the budget level appropriated. By 2007, the number of funded competing training grants should increase, since funding will then be based on turnover from the larger number of grants funded in more recent prior years. ◆

Featured Meetings

This is a list of selected scientific meetings sponsored by NCI and other organizations. For locations and times and a more complete list of scientific meetings, including NCI's weekly seminars and presentations open to the public, see the NCI Calendar of Scientific Meetings at http://calendar.cancer.gov.

NCI Advisory Committee Upcoming Meetings

Date	Advisory Committee
July 12-13	Clinical Sciences and Epidemiology - Subcommittee 1, Board of Scientific Counselors, NCI
July 12	Basic Sciences - Subcommittee 2, Board of Scientific Counselors, NCI
July 12	NCI Board of Scientific Advisors
July 27	Advisory Committee to the Director, NCI

Selected Upcoming Meetings of Interest

Date	Meeting	NCI Speakers
July 8-10	ICT X Satellite Meeting on Molecular Epidemiology—Linking Toxicology to Epidemiology: Biomarkers and New Technologies	Dr. J. Carl Barrett, Director, Center for Cancer Research; Dr. Richard Hayes, Occupational Epidemiology Branch, Epidemiology and Biostatistics Program, Division of Cancer Epidemiology and Genetics
July 10	ASCO Update 2004	Dr. James H. Doroshow, Director, Division of Cancer Treatment and Diagnosis
July 10-13	12th SPORE Investigators' Workshop	Dr. Andrew C. von Eschenbach, Director; Dr. Karen H. Antman, Deputy Director, Translational and Clinical Sciences; Dr. Anna Barker, Deputy Director, Advanced Technologies and Strategic Partnerships; Dr. James H. Doroshow, Director, Division of Cancer Treatment and Diagnosis
July 12-14	Translating Research Into Practice: Advancing Excellence from Discovery to Delivery	Dr. Mark Clanton, Deputy Director, Cancer Care Delivery Systems

NCI Exhibits

NCI Exhibits are presented at various professional and society meetings. Further information about the NCI Exhibits program can be found at http://exhibits.cancer.gov.

This *NCI Cancer Bulletin* is produced by the National Cancer Institute (NCI). NCI, which was established in 1937, leads a national effort to eliminate the suffering and death due to cancer. Through basic and clinical biomedical research and training, NCI conducts and supports research that will lead to a future in which we can 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://cancer.gov.

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