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Genetic Variant May Protect Against Breast Cancer

A consortium of breast cancer researchers reports that a variation in the gene *caspase-8* (*CASP8*) may offer modest protection against the disease. This is the first common genetic variant to be definitively linked to breast cancer, and the researchers believe many others will follow in the years ahead.

The Breast Cancer Association Consortium (BCAC), an international group of about 20 research teams that includes scientists from NCI, made the discovery. Formed in 2005, the Consortium examines genetic associations reported in the scientific literature by pooling data from many studies, including unpublished findings.

The findings appeared online in *Nature Genetics* on February 11.

To assess *CASP8*, the researchers used data on 33,000 women from 14 studies. They found an 11-percent reduction in breast cancer risk among women with a single *CASP8* variant, and a 26-percent reduction among women with two copies of the variant.

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Director's Update

NCI Budget Update

Last Tuesday I gave members of the National Cancer Advisory Board (NCAB) an update on the status of NCI's budget that I'd like to share with the entire cancer community.

Currently, NCI—like many other government agencies supported by the discretionary part of the Federal Budget—is operating under a continuing resolution (CR) which expires on February 15. A CR means current NCI operations are running at fiscal year (FY) 2006 budget levels. The House of Representatives has already passed a revised CR that would cover the remainder of FY2007. That bill will now be considered by the Senate and Congress is expected to pass a new CR under which the government will operate for the remainder of FY2007.

We have been working since last spring to prepare for the FY2007 budget, using the President's 2007 budget proposal, which called for a $40 million, or 0.8 percent, decrease over NCI's 2006 appropriation. This 0.8 percent decrease, plus the percentage decrease which results from inflation, has forced NCI to target reductions of at least an average of 5 percent. The NCI Executive Committee (EC) conducted an exhaustive portfolio review to identify areas where costs could be reduced or programs phased out,

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"Our results indicate that, while many reported genetic associations are spurious false-positives, some associations can be substantiated given a sufficiently large study," says Dr. Douglas F. Easton of Cancer Research UK Genetic Epidemiology Unit and a Consortium leader.

Mutations in genes such as *BRCA1* account for less than 25 percent of the inherited risk of breast cancer. The remainder likely comes from more common genetic variants that individually confer relatively small amounts of risk.

Such variants are thought to play a role in many common diseases. But most single epidemiological studies lack the statistical power required to identify them.

"This study provides proof of principle that consortia like the BCAC are valuable for understanding the contributions of genetic factors in complex diseases," says Dr. Montserrat Garcia-Closas of NCI's Division of Cancer Epidemiology and Genetics and a lead author.

To date, the Consortium has examined about 20 single nucleotide polymorphisms (SNPs). SNPs are locations in the genome where a single unit of DNA may vary from one person to the next.

The researchers caution that epidemiological data cannot prove that the SNP in *CASP8*, called D302H, is causing the reduced risk. They are investigating nearby variants, as well.

D302H is estimated to be present in 13 percent of women of white European ancestry. The new results will lead to studies of *CASP8* in other ethnic groups.

The report has no immediate implications for women. But it suggests that researchers could use the same approach to identify panels of common genetic variants that collectively influence a woman's risk.

"A better understanding of the biology of breast cancer is likely to come from the identification of these variants and future studies that investigate the mechanisms underlying the associations," says Dr. Garcia-Closas.

CASP8 is involved in programmed cell death, a defense mechanism that allows cells to commit suicide rather than develop into a tumor. One hypothesis about D302H is that the variant may enhance the body's ability to clear cancerous cells.

The Consortium examined other genes, as well. They found some support for an association between breast cancer risk and a variant in the transforming growth factor gene *TGFB1*, which helps regulate the growth of cells, among other things.

Numerous variants are likely to be identified in the coming years from genome-wide association studies, says Dr. Jeffery P. Struewing in the Laboratory of Population Genetics at NCI's Center for Cancer Research and a co-author on the study.

Given how few genes have been examined in depth to date, Dr. Easton predicts that large numbers of breast cancer susceptibility variants will eventually be found.

"International collaboration is absolutely essential for these association studies to be successful," he adds. This study included women from 13 countries. ◆

By Edward R. Winstead

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with the goals of accounting for the decreased revenues and creating a pool of money that could be redeployed to new and existing high-priority initiatives or projects.

The EC also completed a comprehensive review of the Office of the Director, which includes almost all of NCI's support structure, with a view to downsizing those programs, as well.

The EC's efforts established a redeployment pool of $60 million. The EC has, by consensus, identified the highest priority programs to receive these redeployment dollars.

However, if there is a CR for the entire FY2007, there may be substantial changes to the budget. For example, the House-passed CR has some important differences from the CR under which we are currently operating, namely, a $620 million increase for NIH over FY2006. It also includes language directing NCI and other Institutes and Centers (ICs) to retain funds that otherwise would have been directed to the NIH Roadmap and elsewhere, and covers part of the cost-of-living increases for federal employees. It further directs the ICs to spend half of the retained funds on competing Research Projects Grants (RPGs) and first-time applicants, setting targets for each.

If these changes are maintained in the bill passed by the Senate, it would provide a slight increase in NCI's 2007 budget over 2006, which would increase the payline and the number of competing RPGs we could fund. Thus, it is possible that NCI will fund approximately 1,310 competing grants in FY2007, an increase of 30 awards. Further details will be provided once the FY2007 budget has been enacted.

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Cancer Research Highlights

Cancer Remains More Lethal to African Americans

"African Americans have the highest death rate and shortest survival of any racial and ethnic group in the U.S. for most cancers," reports the American Cancer Society in *Cancer Facts & Figures for African Americans 2007–2008*. The report cites a number of factors based in economic and social gaps that may contribute to the disparity, including access to insurance, health care, and health education.

The report comes in the context of the second consecutive year of declining cancer deaths, a trend for the overall U.S. population that also applies to the 13 percent who are African American. However, the inequity between whites and African Americans persists, with black men facing a 35-percent greater risk of death from cancer than white men, and black women 18 percent more likely to die of cancer than white women. More than 62,000 African Americans are expected to die of cancer in 2007.

The report also details statistics on risk factors and the use of screening tests, as well as the cancer sites that are most threatening. Lung cancer is the leading killer of both African Americans and whites, though it is more common among African American men and is increasing among African American women. Colorectal cancer strikes African Americans of both sexes more frequently than their white counterparts and is more lethal, as well. Black women are far less likely to have breast cancer than white women, yet far more likely to die from it.

Hematopoietic Drugs During Chemo May Raise Leukemia Risk

To address the diminished supply of white blood cells that results from chemotherapy, patients can receive granulocyte colony-stimulating factors (G-CSFs) or granulocyte-macrophage colony-stimulating factors (GM-CSFs) during treatment. A study led by researchers from Columbia University's Mailman School of Public Health, published February 7 in the *Journal of the National Cancer Institute (JNCI),* shows that these stimulating factors may be linked to an increased risk of subsequent acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS).

The cohort study included 5,501 women aged 65 or older who had received chemotherapy within 12 months of their breast cancer diagnosis. The researchers examined retrospective patient-chart data from the Surveillance, Epidemiology, and End Results program, as well as claims from the Centers for Medicare and Medicaid Services.

They found that women who received either G-CSFs or GM-CSFs were twice as likely to develop AML or MDS as women who did not receive the drugs. The overall incidence, however, was rare: 1.8 percent versus 0.7 percent within 48 months of the treatment.

The authors warn that it's not clear whether these factors caused the leukemia, or whether the higher doses of chemotherapy that often require G-CSFs or GM-CSFs for recovery are to blame, but they note that the risk should be considered for older patients and that more research is needed.

An accompanying editorial goes further: "Only when such studies are coupled to genome-wide single-nucleotide polymorphism analysis or comparable approaches to identify genes involved in leukemia predisposition will it be possible to predict whether G-CSF treatment of normal hematopoietic stem cell donors or cancer patients receiving adjuvant chemotherapy should be avoided in certain individuals."

Heart Attack Mortality Risk Increased After Hodgkin Disease Treatment

British researchers found that patients with Hodgkin disease who were treated with chemotherapy and radiotherapy regimens had an increased risk of death from myocardial infarction, according to study results published in the February 7 *JNCI.*

Dr. Anthony J. Swerdlow of the Institute for Cancer Research in Sutton, UK, and colleagues conducted a collaborative cohort study of 7,033 patients who were registered between November 1, 1967, and September 30, 2000, in the clinical databases of the British National Lymphoma Investigation, the Royal Marsden Hospital, St. Bartholomew's Hospital, and Christie Hospital.

The researchers examined the myocardial infarction mortality risk associated with four treatment regimens: chemotherapy with supradiaphragmatic radiotherapy, chemotherapy without supradiaphragmatic radiotherapy, chemotherapy without supradiaphragmatic radiotherapy

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(Highlights continued from page 3)
or anthracyclines, and radiotherapy without anthracyclines.

Myocardial infarction accounted for 166 of 2,424 cohort deaths, which was more than expected. The mortality risk associated with myocardial infarction was 2.5 times that of the general population of England and Wales. Researchers also found that risks were increased significantly for patients who had been treated with supradiaphragmatic radiotherapy or with anthracyclines or vincristine. However, these results may not reflect the risks for patients currently being treated for Hodgkin disease, as several of the treatments analyzed in this study are no longer in use.

In an accompanying editorial, Dr. John D. Boice, Jr., of the International Epidemiology Institute in Rockville, MD, wrote, "One challenging aspect of the analyses, however, was that so many patients receive both radiotherapy and different combinations of chemotherapy that it is difficult to tease out the contribution of a single agent."

Many Advanced Cancer Patients in Phase I Trials Using CAM

More than one-third of advanced cancer patients enrolled in phase I clinical trials reported using "biologically based" complementary and alternative medicine (CAM) such as vitamins and supplements, a new study reports. The finding, the study's authors argue, suggests that CAM use could be compromising the results of phase I trials.

"We believe our results have potentially serious consequences with regard to the reliability of early phase trial results," wrote lead author Dr. Christopher K. Daugherty and colleagues from the University of Chicago Cancer Research Center.

To conduct the study, the researchers interviewed 212 patients with advanced cancer enrolled in phase I clinical trials at their institution—80 percent of all patients participating in phase I studies there. Patients were interviewed about their use of biologically based CAM. Of the 72 patients who admitted to using such products, approximately half reported taking vitamins and minerals such as vitamins A, C, D, E, selenium, and zinc; the remainder took herbal preparations such as cat's claw, St. John's wort, and echinacea.

CAM users were younger than nonusers, they found, with a median age of 55 years for users compared to 62 for nonusers. In addition, patients with more pessimistic views of their prognosis were more likely to report CAM use.

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FDA Update

FDA Clears Test to Predict Breast Cancer Recurrence Risk

The Food and Drug Administration (FDA) has cleared for marketing a diagnostic test, for use in conjunction with other clinical information and laboratory tests, to assess the recurrence risk for women with early-stage, lymph node-negative breast cancer. The clearance is the first in a category of diagnostic device called an in vitro diagnostic multivariate index assay (IVDMIA).

The test—MammaPrint, developed by the Netherlands-based Agendia—predicts the likelihood of breast cancer returning within 5 to 10 years after a woman's initial cancer diagnosis, based on a microarray analysis of a panel of 70 genes in a sample from a patient's tumor.

The approval follows earlier studies—including a validation study involving more than 300 women published last September in *JNCI*—that showed gene signature scores on MammaPrint were predictive of time to distant metastases and overall survival.

NCI is sponsoring a trial called TAILORx that will use the results of a similar test, Oncotype DX, that measures the activity of a 21-gene panel in tumor samples from women with early-stage, estrogen receptor-positive, node-negative, invasive breast cancer to assign participants to their treatment regimen.

Unlike MammaPrint, explains Dr. Sheila Taube from the NCI Division of Cancer Treatment and Diagnosis, Oncotype DX has been tested on samples from clinical trials and shown to predict the likelihood of a patient benefiting from certain types of chemotherapy as well as of breast cancer recurrence.

Agendia applied for FDA clearance for the MammaPrint test even though it was not required to do so. However, FDA recently released a draft guidance document that suggested tests like MammaPrint and Oncotype DX may require formal FDA approval. Genomic Health, which developed Oncotype DX, currently offers the test under so-called home brew rules that don't require FDA clearance as long as samples are only being tested at a single, company-operated laboratory. The MammaPrint test also is currently conducted only at a single, company-operated laboratory. ◆

Spotlight

Tumor Profiling Moves Closer to the Clinic

A new method of identifying certain cancer-causing mutations in tumors could make it possible for physicians to routinely test for these changes. If the experimental method can be adapted for clinical use, it might be a cost-effective way to identify some of the underlying genetic changes in cancer.

The method is new, but the basic technology is not. Researchers at the Dana-Farber Cancer Institute and their colleagues adapted mass spectrometry genotyping, which has long been used to analyze normal variation in DNA, for the purpose of large-scale tumor profiling.

A pilot study to test the method on 1,000 tumors found it to be a reliable and relatively low-cost way to detect known mutations in cancer-causing genes, or oncogenes. The findings were reported online in *Nature Genetics* on February 11.

"Profiling oncogene mutations with mass spectrometry was not only faster and cheaper but also more sensitive, accurate, and specific than the traditional Sanger method," says former Dana-Farber researcher Dr. Roman Thomas, the first author of the study.

The Sanger method of sequencing DNA is used in laboratories around the world.

The new method could potentially help guide decisions about treatments in real-time, notes Dr. Thomas, who is now a principal investigator with the Max Planck Institute for Neurological Research in Cologne, Germany.

"This is a novel application of a well-established technology that deserves further study" — Dr. Frederic Kaye, NCI

The study was conducted in part because the researchers anticipated a tremendous need to profile large numbers of clinical samples as current and future cancer genome projects neared completion. The profiling would have to be done rapidly and at reasonable cost.

An ideal method would capture information on oncogene mutations across the genome.

The catalog of genetic alterations in cancer keeps growing. Last year, researchers at Johns Hopkins published an analysis of 13,000 genes in colon and breast tumors. They identified 189 mutated genes, most of which had not been linked to cancer previously.

The Cancer Genome Atlas Pilot Project, a large-scale NCI effort, will soon begin to catalog genomic changes in lung, brain, and ovarian cancers.

"We need to know the essential alterations across cancer, but we also need ways to glean the relevant clinical information from every patient who walks through the door," says Dr. Levi Garraway of Dana-Farber, who led the new study.

His team tested the method by screening the 1,000 tumors for the presence of 238 known mutations in 17 oncogenes.

They focused on three types of mutations—those that are common (such as mutations in the *RAS* gene family), those that have clinical implications (such as mutations in the genes *KIT* and *EGFR*), and those that may interact with targeted therapies (such as those in the genes *EGFR*, *KIT*, or *BRAF*).

The tumors that were screened were "high-quality" samples. A potential problem in adapting the method for clinical use is that tumor specimens often degrade when they are preserved in paraffin.

Another limitation of the method is that it detects known mutations. "You have to know what you're looking for," says Dr. Garraway. But the researchers did see several instances of oncogene mutations in tumors where they had never been reported before.

"This told us that if such diagnostics did exist, you could get very useful information on every patient," says Dr. Garraway. Such information could potentially lead to a more focused and effective use of existing and emerging therapies, he adds.

The researchers also identified an unexpectedly high number of co-occurring mutations in some tumors.

An example of how tumor profiling might benefit patients was the discovery of two *KIT* gene mutations in a

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NCI's FY2006 Roadmap contribution was to be $43 million. This, plus the approximately $3 million previously tapped for other uses and the added cost-of-living adjustment dollars, would mean that NCI could have as much as $46 million in FY2007. While we needed $200 million just to stay even, these additional funds will help to address some critical needs.

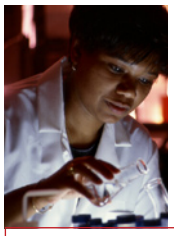
Even though the FY2007 budget is not final, last week the President's FY2008 budget was announced. The NIH President's Budget (PB) request is $28.85 billion, which represents an increase. However, the FY2008 PB request for NCI is $4.78 billion, which is 0.2 percent less than all of the FY2007 budget scenarios. NCI is one of four ICs receiving a decrease and once again we will need to plan for budget reductions for FY2008.

The next step in the process is the House Appropriations Hearing. I am scheduled to accompany Dr. Zerhouni when he testifies on March 6.

As I told the NCAB, there is no question that we have more opportunities than resources to fund them. We are committed to appropriately managing the resources we have and to leveraging those resources by working with partners in the public and private sector.

NCI will continue to make its funding decisions based on science, not target measures of success rates or paylines. Where there is good science, we will do everything we can to support it and ensure the continued progress the cancer community and the American people have come to expect. Nothing less would be acceptable. ◆

Dr. John E. Niederhuber
Director, National Cancer Institute

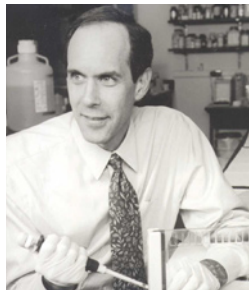


Featured Clinical Trial

Comparing Treatments for Chronic Myelogenous Leukemia

Name of the Trial
Phase II Randomized Study of Imatinib Mesylate at Standard Versus Increased Dose or Dasatinib in Patients with Previously Untreated Chronic Phase Chronic Myelogenous Leukemia (SWOG-S0325). See the protocol summary at http://cancer.gov/clinicaltrials/SWOG-S0325.

Principal Investigators
Drs. Brian Druker and Marilyn Slovak, SWOG; Dr. Peter Emanuel, ECOG; Dr. Martha Wadleigh, CALGB; Dr. Jeffrey Lipton, NCIC



Dr. Brian Druker

Why This Trial Is Important
Development and approval of the drug imatinib (Gleevec) revolutionized the treatment of chronic myelogenous leukemia (CML). CML is usually characterized by a genetic mutation, called the Philadelphia chromosome, that results in the creation of an abnormal protein called Bcr-Abl. Imatinib inhibits the activity of Bcr-Abl, thereby blocking the uncontrolled growth of CML cells and causing them to die.

However, imatinib does not work for some patients, and it sometimes stops working if CML cells develop resistance to it. Therefore, researchers are interested in determining whether the standard dose of imatinib used as initial therapy for CML should be changed, or if a different targeted drug might be more effective.

In this trial, doctors will compare the effectiveness of imatinib at the standard dose versus an increased dose and against a new drug called dasatinib (Sprycel). Dasatinib binds to the Bcr-Abl protein more readily than imatinib and has demonstrated the ability to kill CML cells that have become resistant to imatinib.

"The current standard treatment for CML is 400 mg of imatinib a day," said Dr. Druker, "and that produces a response in about 90 percent of patients. Treatment for this disease is evolving rapidly, however, and newer, more potent drugs are now available. With this trial, we hope to define the best treatment options for patients newly diagnosed with CML."

Who Can Join This Trial
Researchers will enroll approximately 335 patients with previously untreated, chronic-phase CML. See the list of eligibility criteria at http://www.cancer.gov/clinicaltrials/SWOG-S0325.

Study Sites and Contact Information
Study sites in the United States are recruiting patients for this trial. See the list of study contacts at http://www.cancer.gov/clinicaltrials/SWOG-S0325 or call NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237) for more information. The toll-free call is confidential. ◆

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

Notes

OLA Sponsors Understanding NCI Teleconference Series

NCI's Office of Liaison Activities (OLA) is sponsoring its spring "Understanding NCI" teleconference series again this year. The teleconference series is intended to inform the advocacy community and the general public about NCI research and scientific initiatives, as well as featuring an advocate's perspective on the topic.

The first teleconference is scheduled for February 20 from 1:00–2:00 p.m., EST, on "The Importance of the NCI Bypass Budget & Strategic Plan for Patient Advocates" with guest speaker Cherie Nichols, director of NCI's Office of Science Planning & Assessment. Within the U.S., the teleconference can be accessed toll free at 800-857-6584; the passcode is BUDGET. Toll-free playback will be available through March 20 at 800-756-0715.

For additional information, contact OLA at 301-594-3194 or liaison@od.nci.nih.gov.

Missed a Highlight?

The *NCI Cancer Bulletin* Archive allows you to search every issue of this online publication since January 2004. That's more than 100 weeks' worth of articles on a variety of cancer research topics and updates. ◆

AAAS Meets in San Francisco

The annual meeting of the American Association for the Advancement of Science (AAAS) will take place February 15–19 in San Francisco. The theme of "Science and Technology for Sustainable Well-Being" brings together provocative presenters for a wide range of symposia, lectures, and other sessions that address global and national issues in health, energy, the environment, economic development, education, terrorism, science frontiers, and more. For information about the meeting, go to http://www.aaas.org/meetings/Annual_Meeting/. ◆

Funding Opportunities

Administrative Supplements for U.S.-India Bilateral Collaborative Research on the Prevention of HIV/AIDS

Announcement Number: NOT-AI-07-022

Letter of Intent Receipt Date: March 1, 2007

Application Receipt Date: April 18, 2007

For more information, see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=3678. Inquiries: Dr. Kishor Bhatia—bhatiak@mail.nih.gov

For comprehensive information about NCI funding priorities and opportunities, go to http://www.cancer.gov/researchandfunding. ◆

70 YEARS OF EXCELLENCE IN CANCER RESEARCH

If Memory Serves…

NCI's budget in 1938 was $400,000, with $200,000 designated by Congress for the purchase of radium. Within 10 years, the budget increased to $42 million. ◆

For more information about the birth of NCI, go to http://www.cancer.gov/aboutnci/ncia.

(Highlights continued from page 4)

Among the authors' chief concerns about CAM use by patients in phase I trials is their potential to "affect the reliability" of toxicity data. They pointed to the examples of St. John's wort and high-dose vitamin C, both of which "are known to have potentially significant interactions with chemotherapy."

They called for patients being considered for phase I trials to be closely questioned about CAM use. They also suggested excluding patients known to be taking CAM from phase I trials of experimental agents "because they create unknown risks to themselves and other potential trial participants, and lead to potentially unreliable clinical data." ◆

(Spotlight continued from page 5)

gastrointestinal tumor. The patient's tumor had relapsed after treatment with imatinib (Gleevec), and the profiling revealed that one of the mutations was D816H, which is associated with resistance to imatinib.

Physicians who know whether a tumor contains mutations associated with drug resistance may be able to select appropriate therapies for patients.

"This study focused on how best to apply the available information on the biology of the disease to the care of patients," says Dr. Frederic Kaye of NCI's Center for Cancer Research and a co-author of the study.

"This is a novel application of a well-established technology that deserves further study," adds Dr. Kaye. ◆

By Edward R. Winstead

Community Update

Sister Study Seeks Participants

"Woman by woman…sister by sister…we can make a difference."

That slogan is the unifying theme of a unique effort mounted by the National Institute of Environmental Health Sciences (NIEHS), a long-term research project known as the Sister Study. Researchers are recruiting 50,000 women aged 35 to 74, with one crucial trait in common: They all have a sister who developed breast cancer.

Such women are known to be at higher risk of developing breast cancer themselves. Sister Study participants will provide researchers with valuable prospective data because of their links with their sisters: shared genes, a common diet and environment in youth, or even common gene-environment interactions.

Jean Peelen is one of them. In 2001, her younger sister Lynn was diagnosed with breast cancer. "We were all shocked. With no cancer of any kind in our family background, we naïvely thought we were somehow bulletproof," she explains. "Far from it. My older sister Lois was diagnosed a few years ago, and then my older daughter." Both Ms. Peelen and her younger daughter are enrolled in the Sister Study, more committed than ever after Lynn died in 2006. "We still can't explain it," she says. "That's the part that nags at me, and why we are doing our bit to help researchers answer the 'Why me?' question." Ms. Peelen is also actively advocating and helping to recruit older women.

Jean Peelen (center), a participant in the Sisters Study, with her sisters Lynn (left) and Lois (right). Lynn died of breast cancer in 2006 and Lois was recently diagnosed with it.

Though more than 32,000 women have enrolled, researchers are pushing hard to recruit the remaining 18,000 women by the end of 2007. "Many women have heard about the project, but they haven't signed up yet, and we really need them now," says Dr. Dale Sandler, NIEHS Epidemiology Branch chief and principal study investigator. "Physicians know very little about how the environment may affect breast cancer, which is why the Sister Study is so important."

"Women play many important roles throughout their lives—daughter, mother, and friend—but no relationship is as unique as the one between two sisters," explains Sara Williams, part of the recruitment team.

"We're committed to enrolling women in every state, and from all backgrounds, occupations, races, and ethnicities," she comments. "That way, the study results will be widely representative, and of the greatest value."

Organizations partnering with NIEHS on the Sister Study include the American Cancer Society, the National Center on Minority Health and Health Disparities of NIH, Sisters Network Inc., Susan G. Komen for the Cure, the Y-ME National Breast Cancer Organization, and the Intercultural Cancer Council.

The Sister Study Web site is available in English and Spanish, and those interested in joining can determine whether they may be eligible online. For more information go to www.sisterstudy.org, or for Spanish to www.estudiodehermanas.org. A toll-free number is also available: 877-4SISTER (877-474-7837). Deaf/Hard of Hearing: 866-TTY-4SIS (866-889-4747). ◆

Featured Meetings and Events

A calendar of scientific meetings and events sponsored by the National Institutes of Health is available at http://calendar.nih.gov/app/MCalWelcome.aspx ◆

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.

NCI Cancer Bulletin staff can be reached at ncicancerbulletin@mail.nih.gov.