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Gene Model Predicts Recurrence Risk in Early-Stage NSCLC

Researchers have developed a lung "metagene" model that accurately predicts the risk of recurrence for patients diagnosed with early-stage (IA) non-small-cell lung cancer (NSCLC), according to results published in the August 9 *New England Journal of Medicine*.

Previous studies have shown the benefit of adjuvant chemotherapy after surgery for patients with later stages of NSCLC, but not for stage IA disease. However, about 25 percent of patients in that stage subsequently have a recurrence, suggesting a need

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Breaking News

Today, President George W. Bush announced his intention to appoint Dr. John E. Niederhuber as NCI Director. A nationally renowned surgeon and cancer researcher, Dr. Niederhuber joined NCI in September 2005 as chief operating officer and deputy director for translational and clinical sciences, and was named acting director in June 2006. Additional biographical information can be found at http://www.cancer.gov/aboutnci/directorscorner/jen. ◆

Director's Update

Getting New Interventions to Patients More Quickly

There is much excitement in the cancer research community about the rapid discovery of biomarkers. These discoveries range from protein signatures that may predict recurrence or response to therapy, to new imaging technologies that measure the extent of drug-target interactions. The combination of these types of biomarker discoveries with studies that are demonstrating the predictive prowess of gene-expression profiles, like the one highlighted in this week's lead story, is generating tremendous optimism about the future of personalized oncology care.

Of course, advanced technologies have significantly improved our ability to discover potential biomarkers. But biomarker discovery is only the beginning. The harder part is to qualify or validate the biomarker—that is, conduct the clinical studies and develop the correlative data that definitively describe the precise clinical meaning of a given biomarker in a specific situation.

It is for these very reasons—the clinical promise that biomarkers represent and the importance of validating

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to identify a subgroup that might benefit from adjuvant drug treatment, noted the researchers, led by Dr. Anil Potti of the Duke Institute for Genome Sciences & Policy at Duke University.

They combined gene-expression profiles in a cohort of 89 patients with early-stage NSCLC to create a metagene model that predicted the risk for recurrence. "The metagene represents the dominant average expression pattern of the gene cluster across the tumor samples," they explained. In the initial cohort, the lung metagene model predicted disease recurrence with an overall accuracy of 93 percent.

The investigators then evaluated the metagene model in two independent groups of 25 patients from an American College of Surgeons Oncology Group (ACOSOG) study and 84 patients from a Cancer and Leukemia Group B (CALGB) study. The model had an overall predictive accuracy for recurrence risk of 72 percent for the ACOSOG cohort and 79 percent for the CALGB patients. "The lung metagene model was consistently accurate across all the early stages of NSCLC," the researchers reported.

"Our study is a critical first step in the use of genomic tools to refine prognosis and improve the selection of NSCLC patients who are appropriate for adjuvant chemotherapy," noted the investigators.

The metagene model for NSCLC described in the study is similar to a potential genomic strategy for treating early-stage breast cancer, which is being tested in a large clinical study called TAILORx. In that study, a molecular test to analyze the expression patterns of certain genes in a woman's breast tumor that point to a high risk of recurrent disease are used to assign patients to an appropriate treatment regimen.

The researchers in the NSCLC study noted that the refinement of prognosis with the use of the metagene model "provides the opportunity for a prospective, randomized, phase III clinical trial that would evaluate the benefit of identifying a subgroup of patients with stage IA disease estimated to be at high risk for recurrence."

In the proposed study, patients initially classified as having clinical stage IA disease would undergo surgery, and the metagene model would then be used to identify patients predicted to be at high risk for recurrence. "Patients at high risk would then be randomly assigned to observation (the current standard of care for stage IA disease) or adjuvant chemotherapy, in order to evaluate the extent to which the use of genomic reclassification improves survival," the scientists suggested.

Dr. Martin Gutierrez, staff clinician in NCI's Center for Cancer Research (CCR), agreed on the need and value of testing the NSCLC metagene model in a follow-up clinical study. The use of adjuvant chemotherapy for stage I lung cancers "has been controversial," he noted. If the metagene model is confirmed by a phase III study, "it might help identify early-stage patients who are at high risk for relapse and decrease the likelihood of exposing low-risk patients unnecessarily to chemotherapy," Dr. Gutierrez suggested. ◆

By Bill Robinson

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the biomarkers—that, earlier this year, NCI joined with two other Department of Health and Human Services (HHS) agencies, the Food and Drug Administration (FDA) and the Centers for Medicare & Medicaid Services (CMS), to launch the Oncology Biomarker Qualification Initiative (OBQI).

Broadly speaking, OBQI is intended to speed the development and evaluation of new cancer therapies. By bringing together public-private consortia to work on specific projects, OBQI represents the only nationally coordinated effort to validate oncology biomarkers for use in clinical trials.

One specific area of focus is the use of biomarkers as "surrogate endpoints" in clinical trials, meaning that assessments about an intervention's success or failure could be made after several months of treatment, instead of having to wait years to look at more traditional clinical measures. Of course, patients would still be followed to track longer term outcomes and ensure safety, but validated biomarkers that are proven to correlate with treatment response stand to greatly speed the translation of new therapies and technologies from the lab to patients.

An article in last week's issue of the *NCI Cancer Bulletin* explained how NCI is leading an effort to standardize studies to assess whether the results of FDG-PET imaging can be a biomarker of patient response to treatment. Interestingly, one of the first OBQI-supported projects, just recently approved, is a phase III clinical trial that, among several aims, will determine whether FDG-PET can help refine some already established indications of response to treatment for diffuse large B-cell lymphoma (DLBCL).

The trial, being led by CALGB, is important because it is attempting to definitively establish the best treatment protocol for DLBCL, the most common lymphoma type in the United States. Incorporating an FDG-PET biomarker correlative study into this trial (CALGB 50303) represents an important step toward establishing

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Spotlight

Cancer Pain: Helping Patients Help Themselves

Now that extensive research has shown that patients experiencing chronic cancer pain are still not receiving the treatment they need, investigators are focusing their efforts to help patients overcome identified barriers to pain relief.

"About 50 percent of patients who are receiving outpatient therapy for cancer report moderate-to-severe pain. And as the disease progresses, as patients go into the terminal phases of their illness, 80 to 90 percent of those patients report moderate-to-severe pain," explained Dr. Christine Miaskowski, professor of nursing at the University of California, San Francisco, at the NIH Pain Consortium's first annual symposium, held April 17–18 at the NIH campus. "Those percentages…have not changed for 30 years."

Dr. Miaskowski is one of a growing group of researchers who are focusing on patient education as an important component in the fight against cancer pain. In the past, most experimental behavioral interventions designed to improve the treatment of cancer pain have targeted physicians. "And doctors have been responsive," said Dr. Miaskowski. "But the link between the prescription and what the patient is doing with it is the missing piece. You have to also educate the patient and their caregivers."

"If a patient is terrified of becoming addicted, then it doesn't matter if doctors are waiting in line to hand them pain pills—they're not going to take them," explained Dr. Betty Ferrell, a palliative-care researcher at City of Hope Comprehensive Cancer Center in Duarte, Calif., who is also working on education to improve pain treatment. "Overcoming fears and beliefs…is so important before you can move on to try to do something about managing a problem."

For more details on cancer pain relief—including a free copy of the booklet, *Understanding Cancer Pain*—visit NCI's Web site, or call NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237). ◆

Both researchers have developed education-based pain-management programs to be integrated into patients' standard care regimens. In a recent randomized clinical trial, Dr. Miaskowski's PRO-SELF Pain Control Program significantly decreased pain intensity scores and increased the number of appropriate analgesic prescriptions in a group of patients with pain from bone metastases. The PRO-SELF program is based on the concept of academic detailing, which individualizes a teaching program for each patient based on that person's current knowledge and attitudes.

Patients in the PRO-SELF program are given a pain-control booklet, a pain-management diary, a script to help them communicate their pain-management needs, and a pillbox. After identifying the gaps in patients' knowledge, a participating nurse coaches them on timing and frequency of medication intake, how to assess their own pain and response to the medication, how to prevent or treat side effects from pain medications, and how to communicate with their physician about their pain and treatment.

Although the program is still being refined, clinicians have already adapted parts of the PRO-SELF program to their practice, says Dr. Miaskowski. The next step, she explained, is to understand what "dose" of the intervention is most effective. "How long does it take for someone who is dealing with the cognitive questions about taking analgesics to process the information?"

In 2004, to encourage research into new methods to improve symptom management, NCI released a Request for Applications (RFA) titled Reducing Barriers to the Delivery of Symptom Management and Palliative Care. Dr. Ferrell is one of the investigators funded by that RFA. In her project, she and her colleagues have created a hospital-wide system called Passport to Comfort, which incorporates patient education into a comprehensive teaching program addressing patient, professional, and systems barriers to adequate symptom management within the cancer center.

"For example," Dr. Ferrell explained, "a very common thing is that patients believe that if the pain is important then the doctor would ask about it. Patients also don't want to distract the doctor from their underlying can-

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Cancer Research Highlights

Gene Signature Predicts Metastases in Hepatocellular Carcinoma

A team of researchers, including several from NCI, found a unique gene signature in the normal immune cells populating the liver tumor's microenvironment that could predict potential for metastasis, according to a study in the August *Cancer Cell*.

The study included 115 hepatocellular carcinoma (HCC) patients treated at the Zhongshan Hospital in Shanghai, China. Fifty-two patients had tumors that metastasized, and 63 had tumors that did not. In addition, samples from 22 patients with chronic liver disease and 8 patients with normal liver tissues were used as the controls. The researchers used a set of 17 genes, some which encode messages for cytokines, to analyze the gene expression signatures of immune cells in the nearby vicinity of the tumor. Earlier, they had analyzed gene expression within the liver tumors, but the profile from that study could only predict metastasis in 78 percent of the cases.

The latest study identified a unique 17-gene signature in the liver's normal immune cells that could predict if a liver tumor would metastasize in 92 percent of the samples. This unique signature is associated with anti-inflammatory and suppressed-immune responses. These combined activities are associated with a poor prognosis of cancer.

The study's lead author, Dr. Xin Wei Wang of the Liver Carcinogenesis Unit at NCI's CCR said, "This is the first example where we can stratify HCC patients to identify those who would benefit from certain postsurgical treatments to prevent metastases and recurrence."

Breast Cancer Studies Highlight Need to Monitor Cardiac Health

Two new studies suggest that women treated for breast cancer should have their cardiac health monitored if they receive long-term therapy with trastuzumab (Herceptin) or radiation on their left sides. The findings, published early online August 14 in the *Journal of Clinical Oncology*, are particularly relevant to women who may be at risk for heart problems prior to treatment for cancer.

In the trastuzumab study, researchers at the University of Texas M.D. Anderson Cancer Center reported that the long-term use of the drug appears to be safe, but that some patients will develop cardiac toxicity. Forty-nine of 173 women with metastatic HER2-positive breast cancer in the study (28 percent) experienced a cardiac event after taking trastuzumab for at least 1 year.

The toxicity was reversible in the majority of patients, and some patients who experienced a cardiac event were considered for additional treatment with trastuzumab after recovering cardiac function. Trastuzumab is the standard treatment for metastatic HER2-positive breast cancer and, for this population, the overall risk of cardiac toxicity from long-term treatment involving trastuzumab is acceptable, the researchers concluded.

The second study, led by Dr. Eleanor Harris of the Moffitt Cancer Center, examined the long-term effects on cardiac health after irradiation of the breast using contemporary techniques. The researchers found that irradiation of the left breast was not associated with an increased mortality from cardiac disease for up to 20 years after treatment, but it was associated with a higher rate of coronary artery disease and myocardial infarction compared with treatment of the right breast.

The results of this and another study suggest that other known risk factors for cardiac disease may interact with the coronary artery that has been damaged by irradiation and further increase the risk of developing ischemic heart disease after treatment. Women treated for left-sided breast cancer should be monitored over the long term for hypertension and other risk factors, and treated accordingly, the researchers said.

Americans Unclear on When to Get Cancer Screening Tests

While most Americans know that mammograms, Pap tests, and colonoscopies are screening exams for cancer, the majority of Americans do not know the appropriate ages at which initiation of these tests is recommended, according to the latest brief from the Health Information National Trends Survey (HINTS). HINTS, which was developed by NCI, is a nationally representative telephone survey of the general population that was designed to evaluate how the public accesses and uses

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information about cancer, and how this information can be delivered most effectively.

HINTS data collected in 2005 showed that 57 percent of American women were unaware that they should begin to receive mammograms to screen for breast cancer at age 40. Seventy-nine percent of women were unaware that they do not need to have a Pap test yearly to screen for cervical cancer—current general guidelines advise women to get Pap tests at least once every 3 years. Forty percent of all HINTS respondents could not name a test available to screen for colorectal cancer. However, 54 percent did know that screening for colorectal cancer is recommended for men and women age 50 or older, according to general recommendations.

"We must significantly increase our efforts to inform all Americans of what cancer screening tests are available so that we can catch cancer in its earliest stages when it is most treatable," said NCI Acting Director Dr. John E. Niederhuber in response to these results. "We need to get into communities with a renewed education effort."

How Some Tumors Evade Attack by Immune Cells

Researchers have identified a potential mechanism by which some tumors in mice evade attack by antitumor immune cells. Tumors produce a molecule called adenosine that normally serves as a "stop signal" to prevent inflammatory cells from attacking healthy tissue after an infection. The researchers found that when tumors produce adenosine, antitumor T-cell activity is suppressed, and an attack is averted.

"Tumors have hijacked a mechanism that evolved to protect normal tissues from collateral damage that occurs when the body mounts a defense against infection," said lead investigator Dr. Misha Sitkovsky of Northeastern University. Inflammation caused by the host's response to infection triggers the release of adenosine from surrounding cells, which binds to so-called A2A adenosine receptors on immune cells and slows the production of damaging inflammatory molecules.

In the study, the researchers genetically and pharmacologically inactivated A2A adenosine receptors in mice, using various substances, including caffeine, to render antitumor T cells less susceptible to inhibition by tumor-produced adenosine. Most of these mice displayed better antitumor immune responses and delayed tumor growth than mice with intact A2A adenosine receptors, according to findings reported early online this week in the *Proceedings of the National Academy of Sciences*.

"Antitumor T cells that lacked A2A adenosine receptors overcame this type of tumor defense mechanism and inhibited tumor growth in a majority of mice," said co-investigator Dr. Scott Abrams of NCI's CCR. The genetic inactivation strategy was not effective in about 40 percent of the mice, however. One reason may be the existence of other adenosine receptors in these mice; identifying these molecules will be a focus of future research.

HPV16 and HPV18 Variants Related to Race

Genetic variants of HPV16 and HPV18 are linked to a woman's race and the persistence of HPV infection, according to a study in the August 2 *Journal of the National Cancer Institute (JNCI)*.

Researchers from the University of Washington in Seattle analyzed HPV16 and HPV18 nucleotide sequence variations in 1,025 HPV16- and HPV18-positive women. Variants were compared with prototype sequences of HPV16 and HPV18, and were classified as European, Asian, North American, Asian American, African 1, and African 2.

The researchers found that HPV16 and HPV18 African variants were predominant in African American women, while HPV16 and HPV18 European variants were predominant in white women. These variants also are linked to the persistence of HPV infection among different racial groups. HPV16- and HPV18-positive white women with European variants had a greater likelihood of remaining positive for viral DNA than white women with African variants. In contrast, HPV16- and HPV18-positive African American women with European variants had a smaller likelihood of remaining positive for viral DNA than African American women with African variants.

"Given that women with persistent, compared with transient, HPV16 or HPV18 infections are at increased risk of cervical cancer, future studies should be conducted to examine possible mechanisms involving variant-specific immune evasion and their potential clinical therapeutic implications," the authors noted.

In a *JNCI* editorial, Drs. Robert D. Burk and Rob DeSalle stated that because of the unknown link between variants and race, "the 'tangle' is trying to figure out what these factors might be and how the relationships among virus variation, host variation, and persistence lead to cancer." ◆

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cer. To fix that problem, we not only need to teach patients that their pain is important and that they need to let their doctor know about it, but to also coach physicians to broach these topics, because the physicians may be coming from a perspective of 'if the patient has a problem, they'll tell me about it.'"

In addition to incorporating coaching on pain and fatigue management into their clinic for both patients and physicians, City of Hope researchers have worked on increasing awareness within the hospital environment by, for example, placing signs in every examination room, which include: the Passport logo and the message, "We care about your comfort;" the pain and fatigue rating scales; and reminders for patients and physicians to discuss these issues.

Dr. Ferrell's team is currently identifying the components of their system that are most effective, so they can be incorporated into a streamlined second phase. "One of the things NCI is interested in as we develop these interventions is the need to create models that can be replicated in other organizations, and models that are realistic, that can continue even when the study is over."

"We are at a time in 2006 when we have a variety of medications, as well

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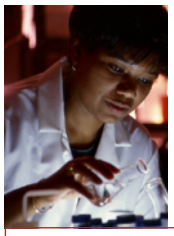
Funding Opportunities

For a complete listing of current NCI funding opportunities, please go to the HTML version of today's *NCI Cancer Bulletin* at http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_081506/page6 ◆

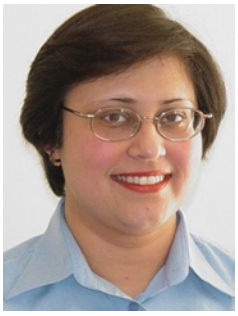


Featured Clinical Trial

Combining Targeted Therapies for Metastatic Colorectal Cancer

Name of the Trial
Phase II Study of Sorafenib and Cetuximab in Patients with Epidermal Growth Factor Receptor-Expressing Metastatic Colorectal Cancer (NCI-06-C-0164). See the protocol summary at http://cancer.gov/clinicaltrials/NCI-06-C-0164.

Principal Investigators
Dr. Shivaani Kummar, NCI's CCR



Dr. Shivaani Kummar

Why This Trial Is Important
Many types of cancer show increased activity or increased amounts of a protein called epidermal growth factor receptor (EGFR). EGFR stimulates cell growth and multiplication in response to other proteins called epidermal growth factors. Cetuximab (Erbitux) is a monoclonal antibody that binds to and blocks EGFR activity.

In this trial, researchers are combining cetuximab with another targeted drug called sorafenib (Nexavar) to treat patients with metastatic colorectal cancer whose tumors show EGFR activity. Sorafenib blocks the activity of two other proteins called vascular endothelial growth factor receptor (VEGFR) and Raf kinase. VEGFR stimulates the growth of blood vessels to tumors (a process called angiogenesis), and Raf kinase is a key molecule in relaying signals from growth factor receptors to the interior of the cell, where the signals are converted into changes in gene activity that lead to cell growth and multiplication.

"The majority of patients with metastatic colorectal cancer have tumors expressing EGFR," said Dr. Kummar. "Cetuximab is approved by the FDA to treat EGFR-expressing metastatic colorectal cancer, but unfortunately, it produces significant tumor shrinkage in only about 10 percent of patients when used as a single agent. With this trial, we hope to see an improved response rate by augmenting the activity of cetuximab with an additional drug that blocks other processes important for tumor growth and cell proliferation."

Who Can Join This Trial
Researchers seek to enroll 53 patients aged 18 or over with metastatic colorectal cancer that tests positive for EGFR. See the list of eligibility criteria at http://cancer.gov/clinicaltrials/NCI-06-C-0164.

Study Site and Contact Information
This study is taking place at the NIH Clinical Center in Bethesda, Md. For more information, call the NCI Clinical Studies Support Center at 1-888-NCI-1937. The call is toll free and confidential. ◆

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

Notes

NCAB to Meet in September

The National Cancer Advisory Board (NCAB) will meet September 5–7 on the NIH campus in Bethesda, Md., in Building 31, C Wing, Conference Room 10. More information will be posted at http://deainfo.nci.nih.gov/advisory/ncab.htm as it becomes available.

NCI to Hold PI Meeting for IMAT Program

NCI has announced its "Seventh Principal Investigators (PI) Meeting for the Innovative Molecular Analysis Technologies (IMAT) Program," to be held September 7–8 at the Bethesda Marriott Hotel, Bethesda, Md. NCI's IMAT program supports research projects to develop and execute pilot applications of novel technologies that will enable the molecular analysis of cancers and their host environment in support of basic, clinical, and epidemiologic research.

The PI meeting will provide a forum for participants to share their ideas and progress, and discuss research and potential collaborations with investigators representing a broad range of scientific expertise. Information on complementary NCI programs and research resources also will be shared, and ideas on how NCI can facilitate progress in developing new molecular analysis technologies for cancer research will be solicited.

Meeting details can be found at http://otir.nci.nih.gov/tech/imat.html.

eHealth Research Conference Slated for September

The "Critical Issues in eHealth Research Conference: Toward Quality Patient Centered Care" will be held September 11–12 at the Bethesda Hyatt Hotel in Bethesda, Md.

The event will provide an interdisciplinary forum focusing on research methodologies that intersect information technology, health communication, behavioral science, medical science, and patient care research; existing and emerging technologies relevant to communications among patients and their health care teams; and conceptual issues related to patient-centered eHealth research.

NCI is sponsoring the conference in collaboration with the American Medical Informatics Association; the Health e-Technologies Initiative (with funding from the Robert Wood Johnson Foundation); and the HHS' National Library of Medicine, Office of Behavioral and Social Sciences Research, Office of Disease Prevention, Agency for Healthcare Research and Quality, and Office of Disease Prevention and Health Promotion.

For more details, go to https://www.ehealth-abstracts.com/Scripts/eHealthHome.asp. ◆

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FDG-PET as a valuable component of clinical trials and improved patient care.

A second project that will be supported under OBQI is a phase II trial to assess whether FDG-PET can predict treatment response in patients with advanced NSCLC.

OBQI's importance is multifold. A truly collaborative effort, it not only will speed drug development, but also will allow FDA to make quicker, more informed decisions about drug approvals, and will enable CMS to make rational coverage decisions for new technologies and interventions. It also will hasten the development of standards, nomenclature, and tools for use in qualifying biomarkers of interest.

Collaborations such as these are no-lose propositions. I expect we will see more like them, and that is good news for cancer researchers and cancer patients. ◆

Dr. John E. Niederhuber
Acting Director
National Cancer Institute

NCI Cancer Bulletin Publication Break

The *NCI Cancer Bulletin* will not be published on August 22 or 29. Publication will resume on September 5. ◆

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as complementary modalities to treat pain; however, many patients with chronic cancer pain remain undertreated," said Dr. Ann Berger, chief of the Pain and Palliative Care Service at the NIH Clinical Center. "The barriers to proper care are many…and an important way of overcoming these barriers is to empower the patient and family to ask for what they need. Much like in the childbirth movement, when patients are empowered and request what they need, the health care system will ultimately be changed, and patients will have their pain adequately treated." ◆

By Sharon Reynolds

Community Update

Breast Cancer and the Environment Research Centers Chart New Territory

Researchers are taking a fresh approach to investigating environmental factors that may be associated with breast cancer risk by focusing on exposure during puberty. Four Breast Cancer and the Environment Research Centers (BCERCs) are exploring whether there are vulnerable times during development of the mammary gland when exposure to environmental agents may influence risk for breast cancer later in life.

"Traditionally, epidemiologic studies of breast cancer and the environment have focused on adult females with breast cancer," said NCI's Dr. Deborah Winn, acting associate director of the Epidemiology and Genetics Research Program (EGRP) in the Division of Cancer Control and Population Sciences (DCCPS). "Early puberty is an established risk factor for breast cancer, and puberty may be an important window of susceptibility to the cancer. These centers are unique in their focus and approach."

BCERCs are enrolling 1,200 girls aged 6 to 8 to examine relationships between breast development, age at first menses, and factors such as hormonal changes, diet, exercise, obesity, family medical history, psychosocial stressors, environmental exposures, and genetic characteristics and biomarkers. In parallel, using rat and mouse models, they are conducting animal studies to characterize the molecular features of the mammary gland over the lifespan and determine how exposure to potential carcinogens during these times influences cancer risk.

Begun in 2003, the research initiative is a 7-year, $35 million endeavor jointly funded by the National Institute of Environmental Health Sciences and NCI. Through DCCPS, NCI contributes 40 percent of this total. Additional support is provided by private organizations.

The centers are located at the University of California, San Francisco, with Dr. Robert Hiatt as principal investigator; the University of Cincinnati, with Dr. Sue Heffelfinger; Michigan State University, with Dr. Sandra Haslam; and the Fox Chase Cancer Center, with Dr. Jose Russo. Each center has a biology and epidemiology component, except Michigan State, which is not participating in the epidemiological study. The centers also have affiliated networks of research and advocacy organizations.

From the outset, breast cancer advocates have been instrumental in the creation of BCERCs and are integral to the project. Each center has a Community Outreach and Translation Core (COTC) comprised chiefly of advocates to translate and disseminate findings, and develop public health messages and other educational materials. Along with COTC, the epidemiology and biology groups work together not only at each center, but also across the centers in their respective areas.

"The centers are structured so that the laboratory research informs the epidemiologic research and vice versa, and consumer involvement is central. Scientists and advocates collaborate throughout the project," said Dr. Winn.

Last month, BCERC members met in Bethesda, Md., to discuss their progress and how to incorporate a transdisciplinary approach to improve their effectiveness. This involves jointly working to integrate discipline-specific concepts, methods, measures, and approaches to produce a new, more powerful conceptual framework for investigating breast cancer etiology.

"The vertical and horizontal integration of science is very much a central topic of focus now at NCI and across NIH," said Dr. Robert Croyle, DCCPS director. "How these centers integrate basic and epidemiologic science and the different types of evidence from each could provide a prototype to use in many different contexts and diseases."

To learn more about the BCERCs, visit www.bcerc.org. ◆

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. Contact the *NCI Cancer Bulletin* staff at ncicancerbulletin@mail.nih.gov.