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Gene Signatures Enhance Breast Cancer Risk Estimates

Combining gene signatures for breast cancer with clinical factors such as patient age and tumor size can improve predictions about the risk of recurrence in women with early-stage disease, new research suggests.

This strategy may also help physicians select the most appropriate chemotherapy regimens for women who undergo additional (adjuvant) therapy to prevent recurrences, the researchers report in the April 2 *Journal of the American Medical Association*.

Gene signatures are characteristic patterns of gene activity in cells that may reflect the underlying disease biology. A number of breast cancer signatures have been developed to predict clinical outcomes and several are being tested in trials such as TAILORx and MINDACT.

Building on this work, researchers at the Duke Institute for Genome Sciences and Policy and their colleagues have now tested the hypothesis that biological information in breast cancer gene signatures is independent of clinical risk factors and that integrating these two sources of information can improve risk assessment beyond traditional methods.

"We can predict who might respond to chemotherapy, but more than that, we can predict which type of chemotherapy may benefit a particular person," says lead investigator Dr. Anil Potti of Duke. "This is truly, in my mind, the next step in personalized medicine."

His team retrospectively analyzed nearly a thousand breast tumor samples for which there was clinical and pathological information. Using this information, they assigned nearly 600 samples to three risk groups: low,

(continued on page 4)

Cancer Research Highlights

Trial Suggests HRT Increases Breast Cancer Recurrence Risk

Long-term follow-up data from a randomized clinical trial indicate that, in women previously treated for breast cancer, use of hormone replacement therapy (HRT) significantly increases the risk of recurrence or contralateral breast cancer—a new cancer in the opposite breast. Published online March 25 by the *Journal of the National Cancer Institute* (*JNCI*), the analysis shows a 2.4-fold increased risk of recurrence or contralateral breast cancer in women randomized to receive HRT to treat menopausal symptoms compared with women given the best, nonhormonal treatments for such symptoms.

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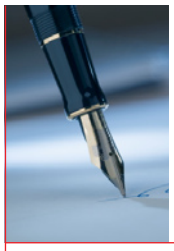


Director's Update

Expanding the Role of Advocates in Shaping, Enhancing Cancer Research

Everything we do at NCI begins and ends with the cancer patient in mind. In our ongoing quest to maintain that focus, NCI is fortunate to receive expert outside advice and recommendations from four federal advisory committees, each offering a unique perspective on how we can best serve patients.

The Director's Consumer Liaison Group (DCLG) brings to NCI the thoughts and concerns of those who have faced cancer, in their own lives and in the lives of those whom they represent. The DCLG is a forum for lay representatives to discuss NCI programs and, together with scientific experts, help develop a shared vision and understanding of today's best science and where tomorrow's research will take us. The ability of DCLG members to understand the science of cancer, the challenges of its complexities, and the opportunities to change the course of disease through investment in science provides NCI with a remarkable tool for communicating NCI's mission and accomplishments.

At the time the DCLG was conceived, NCI's ability to engage members of the cancer advocacy community was limited. Today, in large part because of this board, NCI routinely includes advocates and prepares them to participate in the review of grants, the planning of scientific programs, and the development of educational materials. Yet, there is more we could do together.

Last fall, the DCLG, at my request, convened a working group of advocacy leaders—with widely varying cancer experiences and backgrounds—to recommend how NCI can most effectively involve advocates in our work to help accelerate progress, benefit patients, and improve public health.

"The Director's Consumer Liaison Group brings to NCI the thoughts and concerns of those who have faced cancer, in their own lives and in the lives of those whom they represent."

During last Thursday's DCLG meeting, the Advocates in Research Working Group discussed its progress on a report slated to come before the full DCLG in October. My thanks to the members of the working group, who are putting in many hours and carefully considering better ways we can work together, from the scientific education of cancer advocates to greater participation in and knowledge of clinical trials. The DCLG is uniquely positioned to facilitate communication across the advocacy community, and we have every hope that the working group's report will spark important discussions.

Last year, recognizing the importance of the advocacy community, NCI realigned the Office of Advocacy Relations (OAR), bringing it into the Office of the Director. Acting on a charge to enhance NCI's relationships with our external stakeholders, OAR is, today, closely considering how it forges connections between NCI and the advocacy community, at both the individual and organizational levels, and how we can do better. A cornerstone of these connections is the DCLG. We need the DCLG to be a strategic partner, informing NCI activities and coordinating support activities in the community.

To that end, we must utilize the DCLG as an important resource, for NCI and for the National Cancer Program. We have long talked about the need to focus on our common interests rather than accentuate our differences. It is a message that bears frequent repetition. Indeed, if we are going to make a difference in the course of these diseases, we must be united in purpose and speak with a common voice.

The DCLG, along with NCI's other advisory boards, will be a key player in disseminating this message of unity and working together across the diverse cancer community to enhance the efficacy of our vast cancer research enterprise and its ultimate goal of changing the face of cancer. ◆

Dr. John E. Niederhuber
Director, National Cancer Institute

Cancer Research Highlights

(continued from page 1)

The trial, called HABITS, conducted in Scandinavia, was halted in 2003 after an interim analysis showed a 3.5-fold increased risk of cancer in women in the HRT arm. This longer-term analysis followed 442 women for a median of 4 years. Of the 221 women in the HRT arm, 39 had a "breast cancer event," compared with 17 of 221 in the control arm.

The results "suggest that [HRT] not only induces and promotes breast cancer, but also may stimulate the growth of tumor microdeposits in breast cancer survivors," concluded the study's lead author, Dr. Lars Holmberg from the King's College London School of Medicine, and colleagues.

Several observational studies have found no increased recurrence risk among breast cancer survivors taking HRT. However, the authors argued, "The majority of these observational studies were not formal studies that could control sufficiently for bias and confounding."

In addition, a similar randomized trial launched in Sweden at about the same time as HABITS showed a decreased risk of breast cancer recurrence associated with HRT. The two trials had several design differences that could account for the discrepancies, the researchers noted, including the use among many HABITS participants of a more potent progestagen in their HRT regimen. (No single HRT type was prescribed for the trial.)

In a related commentary in *JNCI*, Dr. Kathleen Pritchard from Sunnybrook Odette Cancer Center in Toronto, Canada, indicated that the HABITS data are convincing.

"It seems that the harmful side effects of HRT [in breast cancer survivors] have finally been clearly demonstrated in what is, by today's standards, a small randomized trial, carried out in a few relatively small countries," Dr. Pritchard wrote.

Vaccine Treats Breast Tumors in Mice

A new therapeutic vaccine designed to stimulate the body's immune system so that it recognizes cancer as an invader shows promise in eradicating some advanced breast cancer tumors in mice. The study results appeared March 15 in *Cancer Research*.

The research team, led by Dr. Jay Berzofsky of the Vaccine Branch in NCI's Center for Cancer Research, engineered a vaccine using a modified adenovirus to code for portions of a protein called neu, which corresponds to human epidermal growth factor 2 (HER2) in humans—a surface receptor overexpressed in 20 to 25 percent of women who have breast cancer.

Mice were injected with mouse breast cancer cells called TUBO cells to generate tumors with high levels of neu. When the TUBO cells and vaccine were given at the same time, no tumors formed. When the vaccine was given after the TUBO cell injection, small tumors formed, but they disappeared within 45 days and did not reappear.

The larger the tumor load, the more difficult it was for a vaccine-induced immune response to cause these tumors to shrink and disappear. Tumors up to 2 cubic centimeters continued to grow for a week after immunization but disappeared within a month. Even tumors up to 3.5 cubic centimeters eventually disappeared. But tumors that were 5.5 cubic centimeters at the time of vaccination resumed growth after initial shrinkage.

The sooner the vaccine was given after TUBO cell injection, the lower the incidence of metastasis to the lungs, as well. With metastasis, it took longer for the immune response to clear the cancer if a large number of tumors were present. Mice with more than 200 metastases were tumor-free within 38 days.

"A vaccine offers several advantages over a monoclonal antibody treatment, which targets a single region on a receptor," said Dr. Berzofsky. "A vaccine may induce the production of several different antibodies and target multiple regions on a receptor, making it harder for the tumor to mutate and escape the effects of therapy."

Dr. Berzofsky added, "These results in mice show the potential for producing a vaccine that induces antibodies to an overexpressed cell surface receptor such as HER2 in breast cancer patients."

Guidelines for Colonoscopy Follow-up Assessed

The size and number of polyps removed during colonoscopy may be of limited use in predicting a recurrence that leads to cancer, new research suggests. The findings, in the March 18 *Annals of Internal Medicine*, raise questions about the

(continued on page 4)

(Highlights continued from page 3)
current guidelines on follow-up colonoscopies, which define a schedule for surveillance exams based on detected polyps, or adenomas.

For patients with an advanced adenoma—considered high risk for becoming cancerous—or with at least three adenomas, the guidelines recommend follow-up within 3 years. For patients with fewer, nonadvanced polyps, repeat exams are recommended in 5 to 10 years. Surveys show, however, that many physicians schedule follow-up colonoscopies earlier than the guidelines suggest.

One reason may be that the guidelines have not been assessed in a prospective study. To explore this question, Dr. Adeyinka O. Laiyemo of NCI's Division of Cancer Prevention and his colleagues studied 1,905 patients in the Polyp Prevention Trial. Participants had an adenoma removed at baseline and underwent repeat colonoscopy at 1 year and 4 years.

In this study, the risk stratification model used in the current guidelines did not reliably predict the recurrence of advanced adenomas. Overall, 6.6 percent of participants had an advanced adenoma recurrence at 4 years. The advanced adenoma rates were 9 percent and 5 percent in patients with high-risk and low-risk adenomas at baseline colonoscopy, respectively.

An editorial accompanying the paper notes that while this difference is statistically significant, it may not be meaningful to patients and clinicians, given that the predictive accuracy of the current risk model is only 71 percent. (By contrast, the predictive accuracy of flipping a coin is 50 percent.)

Dr. Laiyemo stresses the need for more reliable tools to identify individuals at the highest risk for advanced adenoma recurrence. The misclassification of cases may mean that preventable colon cancers are missed or that limited medical resources are allocated poorly.

The researchers also found that patients are at high risk if they have two adenomas and one is on the right side of the colon, near the small intestine. The reason for this apparent association, which has been suggested in other studies, is not yet clear.

Oncogene Identified in Diffuse Large B-Cell Lymphoma

Researchers have identified how mutations in a gene called *CARD11* contribute to cancer cell survival in a type of diffuse large B-cell lymphoma (DLBCL) with poor prognosis, called activated B-cell-like (ABC) DLBCL. The study results, published March 21 in *Science*, identify *CARD11* as a possible future target for new therapies.

To prevent cell death, malignant ABC DLBCL cells rely on the nuclear factor-kappa B (NF-κB) signaling pathway—a cell-signaling pathway that plays an important role in cell proliferation, differentiation, and survival. NCI researchers previously reported that *CARD11* stimulates abnormal cellular signaling of the NF-κB signaling pathway in ABC DLBCL. However, the underlying mechanism for this abnormal cellular signaling was not known.

To determine how *CARD11* contributes to cancer, the researchers sequenced the gene in samples taken from ABC DLBCL biopsies and cell lines. They found that all of the *CARD11* mutations coded for a region of the CARD11 protein called the coiled-coil domain.

As determined by fluorescence microscopy, mutant CARD 11 proteins were more likely to aggregate (bunch together), and the degree of aggregation correlated with the protein's ability to activate the NF-κB pathway, thereby helping malignant cells survive. In a set of experiments using small hairpin RNAs to knock out mutant *CARD11* function, cells from an ABC DLBCL line with mutant *CARD11* died when the gene was blocked; these cells were not saved when researchers introduced a normal *CARD11* gene, indicating an "addiction" to the mutant signaling pathway.

"Our results demonstrate that *CARD11* is a bona fide cancer-causing gene in DLBCL, thus providing a genetic rationale for the development of drugs that could block the CARD11 pathway," concludes Dr. Louis Staudt from NCI's Center for Cancer Research, senior author of the study. ◆

(Gene Signatures continued from page 1)
intermediate, and high.

The researchers then used gene signatures to further stratify the probability of recurrence among each risk group. The signatures include well-characterized genes involved in cell communication and other molecular pathways that are deregulated in the disease. The result was "clusters" of patients with a range of clinical outcomes, and the clusters were confirmed in 391 additional samples.

The researchers plan to validate the strategy in several prospective trials. The current results reflect the limitations of a large, retrospective study, which included tumor samples from different studies and in some cases lacked complete clinical data.

For instance, the status of the *HER2*
(continued on page 10)

Special Report

Lung Cancer Test Aims to Improve Early Detection

When an imaging test shows a suspicious mass in the lungs of a smoker, the next step is a bronchoscopy. A thin tube with a camera is passed into the person's airway to look for abnormalities and collect tissue for biopsy. But in many cases the results do not reveal whether the person has cancer.

At this point, a physician may decide, based on the available evidence, to pursue more invasive testing or to monitor a patient—a "watch and wait" approach. Unfortunately, there are no validated diagnostic tests or biological markers that reliably distinguish between smokers with and without the disease.

Researchers in Boston hope to change that. They have developed a genomic test that analyzes the activity of 80 genes in cells from a patient's airway. The airway cells, which can be collected during bronchoscopy, appear normal under the microscope, but they may have abnormal patterns of gene activity associated with lung cancer.

The test is based on the idea that toxins in cigarette smoke alter the behavior of genes throughout the respiratory tract—not just in the tumor—and that these changes have diagnostic value.

"The goal of this research was to identify gene expression patterns that can distinguish smokers with and without lung cancer," said Dr. Avrum Spira of Boston University School of Medicine, who co-led the project.

Preliminary results reported last year showed that the genomic test and bronchoscopy together were a better predictor of lung cancer than either test alone. There were even hints that the combination may improve the detection of small lesions or early-stage cancers—the ones more likely to respond to therapies and most often missed by bronchoscopy.

Dr. Spira discussed the test last month at the annual meeting of the NCI-sponsored Early Detection Research Network. A theme of the meeting was the need for biological markers with clinical relevance, as the lung cancer genomic test aims to be. EDRN and Dr. Spira are discussing ways to move this test towards clinical validation.

"This test addresses a serious dilemma in the clinic," said co-investigator Dr. Marc Lenburg of Boston University. "It's a real-world problem."

The need for better diagnostic tools is clear. Bronchoscopy detects stage 1 lung cancer in only 15 to 20 percent of cases, so physicians must move on to more invasive and more expensive tests, including exploratory surgeries, to determine if the lesions they see are cancer, according to Dr. Jerome Brody, who directs the Boston University Pulmonary Center and helped develop the genomic test.

As with all biomarker candidates, the 80-gene signature is experimental and must be validated in a large, well-designed study. A trial is being planned to evaluate the genomic test in 300 patients in the United States and Europe.

The validation study will also explore whether the genomic test can help physicians identify the subtype of lung cancer a person has and the underlying genetic flaws. This information could help physicians identify the most appropriate therapies for patients.

All three researchers have financial interests in a company called Allegro Diagnostics, which has raised funds to validate and extend this study and to make the test available commercially.

The researchers describe their approach as a "clinicogenomic" prediction model. In a study published online yesterday in *Cancer Prevention Research*, they say that the clinical and genomic information is both complementary and synergistic.

"What's new here is the combining of the genomic data with clinical information to develop a statistically valid predictor of lung cancer," said Dr. Brody, who was not an author of the most recent study. "This is one of only a few studies in any cancer that has attempted to combine the two in a statistically valid fashion."

The prediction model may expedite more invasive testing and appropriate therapies for smokers with lung cancer and reduce invasive diagnostic procedures for individuals without lung cancer, the authors conclude. ◆

By Edward R. Winstead

A Closer Look

Managing Bone Metastases: Can Radiopharmaceuticals Help?

When cancer spreads to bone during the advanced stages of disease, the results can be devastating. Some patients experience severe pain and face an increased risk of fractures and other skeletal-related complications. These often require additional treatments and may further diminish a patient's quality of life and compromise survival.

As systemic anticancer therapies improve, the problem of bone metastases is likely to become increasingly common, and new, cost-effective therapies are needed. Toward this end, a strategy aimed at preventing or delaying skeletal-related complications from bone metastases is being evaluated in a prospective, randomized NCI-sponsored clinical trial.

The researchers are testing whether a drug called zoledronic acid (Zometa), a standard therapy for patients with bone metastases, is more effective when given with a radiopharmaceutical such as Strontium-89 or Samarium-153. Radiopharmaceuticals are bone-seeking radioactive agents that incorporate into areas of bone being turned over by metastases.

The beauty of radioisotopes, which are administered intravenously, is that they target all bone metastases with a low concentration of radiation in the surrounding normal bone marrow and other structures, according to the researchers.

"If a patient has 30 to 40 spots on an affected bone, the radioisotope would go to all of the sites," said co-principal investigator Dr. Michael J. Seider of Summa Health System Hospitals in Akron, OH. "It is a fast, simple, and relatively non-toxic drug."

The trial, Dr. Seider noted, is asking a simple question: "If we add a radioisotope to a drug that already works in delaying skeletal-related events, will we further delay these skeletal-related events?"

The randomized, phase III study is enrolling patients with three cancers that commonly spread to bone—lung, breast, and prostate. To enroll in the study, participants must have bone metastases but no significant bone pain. All participants will receive zoledronic acid as a primary treatment and half will receive a single dose of a radioisotope. (The trial presumes that either radioisotope is acceptable for treatment.)

Participants will be followed for the development of pain and skeletal-related complications. During the trial, patients may receive any other type of therapy, including cytotoxic therapy, hormone therapy, or additional radiation therapy (except for treatment of bone metastases).

This point is critical because there is a misperception, particularly among some medical oncologists, that patients taking radioisotopes cannot receive other therapies at the same time. Studies have shown, however, that radioisotopes can be given with other therapies without causing more side effects than other combination therapies.

"We need to debunk the misconceptions and fears that exist regarding radiopharmaceuticals," said co-lead investigator Dr. Corey Langer of the Fox Chase Cancer Center. "The big problem with this class of drugs is the false impression that once you give them to patients their marrow function never recovers. We certainly are not seeing that in this trial."

To date, the trial has enrolled more than 50 of a planned 352 participants. It includes a component that will measure quality of life. Another question is the cost effectiveness of the combination therapy, because delaying the need for additional treatments for skeletal-related events could prevent expensive procedures.

If the trial is successful, noted Dr. Langer, the combination therapy could improve the lives of many patients with bone metastases by minimizing their pain and delaying further complications.

The current challenge is to overcome the notion that giving radioisotopes would prevent patients from getting any other type of therapy. "If we can break through this misconception, the study looks to be very promising," said Dr. Seider. ◆

By Edward R. Winstead

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_040108/page7. ◆

Spotlight

Flat and Depressed Colorectal Growths May Change Screening

Unlike most cancers, colorectal cancer is considered preventable in many cases: prevailing opinion states that many malignancies found in the colon or rectum began years earlier as adenomas—noncancerous tumors that form in the linings, or mucosa, of these organs. Early detection and removal of these adenomas is the basis of screening for colorectal neoplasms.

Traditionally, doctors have focused on finding and removing polypoid adenomas—growths that protrude from the mucosa—during screening colonoscopy. But newer evidence suggests that flat (having a height less than half of the diameter) or depressed adenomas may be even more likely to harbor precancer or cancer, and may be more common than previously realized.

In a recent study published in the *Journal of the American Medical Association* (*JAMA*), investigators examined 1,819 patients undergoing colonoscopy for screening, surveillance, or symptoms of colorectal neoplasms. Although just over 9 percent of adenomas found were flat or depressed (known as nonpolypoid), these growths accounted for about 15 percent of identified neoplasms and 54 percent of high-grade dysplasia and submucosal invasive carcinoma in this series of patients.

Advanced cancers that arise from nonpolypoid adenomas are indistinguishable from those that arise from polyps. "If we had not intervened, if we had missed [the nonpolypoid adenomas], some of them would have become invasive cancers, and by that time we wouldn't know where they had come from, because they would have gone through the transformation to become bulky and invasive," says Dr. Roy Soetikno from the Veterans Affairs Palo Alto Health Care System and Stanford University, lead author of the *JAMA* study.

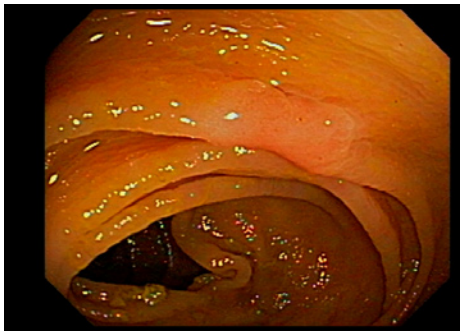


Image of a nonpolypoid colorectal adenoma taken during colonoscopy

The overall prevalence of nonpolypoid colorectal neoplasms (NP-CRN) in the general population remains unclear, and scientists do not know if these types of adenomas grow or recur faster than the more common polypoid lesions. In an editorial accompanying the paper in *JAMA*, Dr. David Lieberman from Oregon Health and Science University writes that polypoid and nonpolypoid neoplasms missed during screening "may represent the most common explanation for interval cancers," that is, cancers that arise in between scheduled colonoscopies or other screening tests.

However, explains Dr. Barry Kramer, associate director for disease prevention at the National Institutes of Health, "we really don't know, because we really can't be confident about the natural history of these lesions. All we have at this point are cross-sectional studies; that is, what appears in the colon at the time of colonoscopy or sigmoidoscopy. If we're aware of polyps or flat adenomas [during screening], we take them out. And so we lose our ability to learn, at least with precision, what the natural history is.

"That's a gap in our knowledge at this point," he continues. "It will also be useful to know if there are differences in the molecular fingerprints between these lesions and the usual [polypoid] adenomas. If there are, that might help us predict the behavior of a given lesion, and that's an important area for research."

Two traits of NP-CRN agreed on by investigators are that they are more difficult to detect and more difficult to remove. Unlike polyps, which can be cut away from the intestinal wall fairly easily, removing NP-CRN involves a multi-step procedure called mucosal resection.

By training with Japanese endoscopists and studying videos of NP-CRN cases, Dr. Soetikno's team learned to look for the characteristic features of NP-CRN, which include a slightly red appearance, altered or absent vascular network, friability, and wall deformity. He believes that any interested physician can learn to recognize the lesions. "You need to have an imprinting of the shapes, of the color, in your mind…if people are willing to spend the time and look at [training] movies and really imprint them in their minds, I think people can learn."

(continued on page 8)

(Spotlight from page 7)

His research group plans to make their training materials available to interested endoscopists through the American Society for Gastrointestinal Endoscopy. "The technique of mucosal resection also needs to be disseminated, so the benefit of finding these flat lesions can be maintained," he adds.

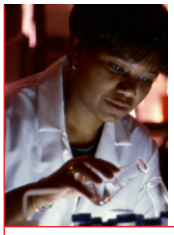
Another screening test called virtual colonoscopy—also known as CT colonography—which uses computed tomography (CT) to visualize the GI tract noninvasively, has been tested recently in clinical trials.

While researchers are debating how to optimize CT colonography to better detect truly flat or depressed lesions, Dr. Perry Pickhardt, associate professor of radiology at the University of Wisconsin Medical School, believes that most "lesions the *JAMA* paper describes are things that we see routinely, and with current techniques we really don't have much problem finding those lesions. I think awareness is the main thing, and that's a very important message: be aware of these."

"We're still developing techniques to optimize both colonoscopy and CT colonography…as there's increasing awareness that [nonpolypoid lesions] exist and are relatively common," says Dr. Kramer.

"The future of screening for colorectal neoplasms is to detect and remove all neoplastic lesions: polypoid and nonpolypoid. By having data to show the existence and importance of the flat and depressed lesions in the United States, we can alert all endoscopists," said Dr. Soetikno. "Our patients, referring physicians, and insurers expect that when we give a patient a clean bill of health, we do not leave any neoplasms behind." ◆

By Sharon Reynolds



Featured Clinical Trial

Batracylin for Patients with Advanced Solid Tumors or Lymphoma

Name of the Trial
Phase I Study of Batracylin in Patients with Metastatic or Unresectable Solid Tumors or Lymphoma (NCI-07-C-0097). See the protocol summary at http://cancer.gov/clinicaltrials/NCI-07-C-0097.

Principal Investigator
Dr. Martin Gutierrez, NCI Center for Cancer Research

Dr. Martin Gutierrez

Why This Trial Is Important
Scientists have made great strides in determining how certain proteins contribute to cancer formation, growth, and spread. As a result, the development of drugs that target these proteins has become a major focus of cancer research.

Along with the development of such targeted therapies, researchers have explored the possibility of matching the genetic characteristics of patients to treatments that may be especially suited to them. The drug batracylin is an example of a targeted therapy that may prove beneficial to patients with certain genetic characteristics.

Batracylin inhibits two proteins, topoisomerase I and topoisomerase II, that are overabundant in certain types of cancer cells and may play a role in cancer formation and progression. Drugs have been developed that target one or the other of these proteins, but batracylin is the first drug to reach human clinical trials that targets them both.

Although this ability makes batracylin a promising anticancer agent, early testing in animals indicated that different species process the drug differently, with some species processing it very quickly, resulting in unacceptably severe side effects. Subsequent research showed that a cellular process called acetylation occurs more rapidly in these species, causing them to process batracylin more quickly. This finding led researchers to theorize that humans whose genetic characteristics cause slow acetylation would be able to tolerate and benefit from treatment with batracylin.

In this trial, patients with solid tumors or lymphomas for which standard therapies do not exist or are of minimum benefit and who are slow acetylators, as determined by a blood test, will be treated with increasing doses of batracylin. Researchers hope to assess the pharmacokinetics of batracylin in these patients and determine the most appropriate dose for future clinical trials.

For More Information
See the list of entry criteria and trial contact information at http://cancer.gov/clinicaltrials/NCI-07-C-0097 or call the NCI Clinical Trials Referral Office at 888-624-1937. 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

Teleconference About CCOPs Slated for April 10

The next "Understanding NCI" teleconference will take place on April 10 from 2:00 to 3:00 p.m., EDT. The topic is "Clinical Trials in Your Community: NCI's Community Clinical Oncology Program (CCOPs)." The call will feature Dr. Lori Minasian, chief of NCI's Community Oncology and Preventive Trials Research Group; Dr. John Kugler, a principal investigator with the Illinois Oncology Research Association CCOP; and Ms. Laura Matus, volunteer coordinator of Illinois Cancer*Care*.

Within the U.S., the teleconference can be accessed toll-free at 800-857-6584; the passcode is: Prevention. Toll-free playback will be available through May 10 at 800-284-7027.

To learn about the "Understanding NCI Teleconference Series" and to learn about past teleconferences, please visit: http://advocacy.cancer.gov/.

DCLG Seeks New Members for 2008

The NCI Director's Consumer Liaison Group (DCLG) is now accepting applications for up to six new members. Applications must be postmarked by April 30.

The DCLG is a federally chartered advisory committee of the NCI. It consists of 16 consumer advocates who are involved in cancer advocacy and who reflect the diversity among those whose lives are affected by cancer. The mission of the DCLG is to advise, assist, consult with, and make recommendations to the NCI Director, from the perspective and viewpoint of cancer consumer advocates on a wide variety of issues, programs, and research priorities. The DCLG serves as a channel for consumer advocates to voice their views and concerns.

Please visit the DCLG Web site at http://dclg.cancer.gov/membership/nominations for information on the application process and to view eligibility requirements.

Free Telephone Workshop Series for Cancer Survivors

The sixth annual telephone workshop series, "Living With, Through, and Beyond Cancer," begins April 22. This series offers cancer survivors, their families, friends, and health care professionals practical information to help them cope with concerns and issues that arise after treatment ends.

The program is a collaborative effort between NCI, Cancer*Care*, the Lance Armstrong Foundation, the Intercultural Cancer Council, Living Beyond Breast Cancer, and the National Coalition for Cancer Survivorship.

The workshops are free; no telephone charges apply. To register, visit the Cancer*Care* Web site at www.cancercare.org/TEW. All workshops will take place on Tuesdays from 1:30 p.m. to 2:30 p.m. EDT on the following dates:

Part I: "The Importance of Communicating with Your Doctor about Follow-Up Care," April 22

Part II: "Rediscovering Intimacy in Your Relationships Following Treatment," May 13

Part III: "Survivors Too: Family, Friends, and Loved Ones," June 24

DCLG Remembers Kerry Dewey

Ms. Kerry Dewey, a founding member of the Director's Consumer Liaison Group (DCLG), died March 10 after a long struggle with breast cancer which was first diagnosed in 1984. She was 56 years old and lived in Missoula, MT.

After her diagnosis, Ms. Dewey became a patient advocate. She was a trainer with the American Cancer Society Reach to Recovery program and she initiated and led several support groups, including a peer support group for spouses, partners, and male family members called "Male Call." Due to her advocacy work and efforts to develop a statewide resource for patients and families called *The Montana Breast Cancer Resource Guide*, she was selected as a member of the DCLG in 1997 and served until 2001.

Mr. Mike Katz, a former DCLG chairperson, said of Ms. Dewey: "Kerry was one of our committee's most impactful members. She was wonderfully soft spoken, with a lovely sense of humor. She sometimes single-handedly brought our most outspoken advocates from the big metro areas back to earth about the unique challenges faced by cancer patients in rural areas. There isn't anyone who met her who didn't come away with a special affection for a person who was clearly one of Missoula's finest and one of its most effective ambassadors."

(continued on page 10)

(Notes continued from page 9)

NCI Issues Colorectal Cancer Progress Report

NCI recently released a colorectal cancer progress report, *Colorectal Cancer: Six Years of Research Progress*. This retrospective analysis addresses the Colorectal Cancer Progress Review Group's recommendations on the most urgent needs and promising directions for future NCI investment in the areas of colorectal cancer biology, etiology, prevention, early detection and diagnosis, treatment and prognosis, and cancer control and survivorship. The report includes current trends in colorectal cancer incidence, mortality, and screening and provides the number of NCI-funded colorectal cancer research projects and clinical trials. The report also highlights initiatives and research advances selected by colorectal cancer experts from across NCI. To view the progress report, go to http://planning.cancer.gov/disease/2008colorectal.pdf.

National Smoking Cessation Campaign Launched

On March 31, an alliance of public health organizations launched *EX*, a public health campaign to promote a single smoking cessation message to the public, guide smokers to existing cessation resources, and build their confidence about quitting.

The program consists of paid TV, radio, and internet ads; a Web site (www.BecomeAnEx.org); and a free quit plan book. The *EX* program also includes a research component. The *EX* Smoking Cessation Panel Study will collect survey data via telephone interviews with adult smokers over a 2-year period.

NCI is participating in this effort by providing funding to assist with the evaluation of *EX*, which was launched by an alliance of the nation's leading public health organizations and 14 states called the National Alliance for Tobacco Cessation (NATC). Members of the NATC include the American Cancer Society, the American Heart Association, the American Legacy Foundation, the Robert Wood Johnson Foundation, the Association of State and Territorial Health Officials (ASTHO), the Mayo Clinic, and others. ◆

(Gene Signatures continued from page 4)

gene, which can affect prognosis, was not always known. Another limitation was the small number of patients within certain clusters, which hindered statistical comparisons.

It is only through very large studies that the true genetic diversity of breast cancer will be revealed, notes Dr. Chiang-Ching Huang of Northwestern University, who coauthored an accompanying editorial.

"Cancer is heterogeneous, and you cannot see the subtypes or the differences in the risk of relapse and responses to therapy in small numbers of cancers," says Huang. "This study shows that if we pool our efforts we can get large enough samples to see if there are real signatures with prognostic power."

With so many experimental gene signatures for breast cancer, what the field needs now are studies to assess these classifiers in concert, says Dr. Lisa Anne Carey of the University of North Carolina Lineberger Comprehensive Cancer Center, who was not involved in the research.

Such studies may further document genetic alterations in breast cancer subtypes and eventually lead to clinical tools.

"This is intriguing work that begs to be taken further," says Dr. Carey. ◆

By Edward R. Winstead

Meet NCI Experts at AACR

Learn about NCI's programs and Web sites by visiting Booth #1120 in the exhibit hall during the American Association for Cancer Research Annual Meeting. NCI experts will be available to talk about a wide range of topics. See the schedule below.

MONDAY, APRIL 14

10:00–11:00
Small Business Innovations Research and Technology

1:00–2:00
Cancer Complementary and Alternative Medicine Research at NCI

TUESDAY, APRIL 15

11:00–12:00
The Alliance for Glycobiologists for the Detection of Cancer and Cancer Risk

12:00–1:00
Early Detection Research Network (EDRN): Investment in Biomarker Research

FEATURED AT THE NCI EXHIBIT

Get detailed information about these programs and offices:

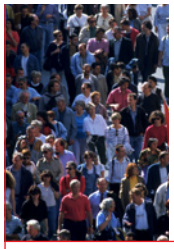
Center for Cancer Research

Division of Cancer Epidemiology and Genetics

Division of Cancer Prevention

Center to Reduce Cancer Health Disparities

Cancer Prevention Fellowship Program ◆



Community Update

U.S. Military Health Program Provides Coverage for NCI Clinical Trials

Effective today, the U.S. Department of Defense's (DoD) TRICARE health care program and NCI have renewed their interagency agreement to provide TRICARE beneficiaries with more options for cancer care and greater access to advances in cancer prevention and treatment through clinical trials. The decision is based on a successful 10-year DoD-NCI demonstration project in which more than 800 members of the armed forces and their families have participated in NCI trials.

U.S. Assistant Secretary of Defense for Health Affairs Dr. S. Ward Casscells noted: "We hope this continued partnership in cancer clinical trials will raise awareness among our TRICARE cancer patients that clinical trials are a promising treatment option and encourage them to consider clinical trial participation."

NCI Director Dr. John Niederhuber concurred: "One of NCI's highest priorities is to ensure that our latest science—new treatments and new prevention methods—is available to all patients in the communities where they live. Our agreement with TRICARE helps advance that goal." He also expressed hope that TRICARE's actions will serve as a model for other health insurers to add or expand their beneficiaries' coverage of NCI- and other NIH-sponsored clinical studies.

TRICARE's benefit allows the program's 9.2 million beneficiaries to take part in phase II and phase III NCI-sponsored cancer clinical trials, including studies for prevention, screening, early detection, and treatment. All medical care for trial participants will be provided by Military Treatment Facilities (MTFs) or civilian providers participating in NCI-sponsored studies. In a press release, TRICARE noted that there are more than 2,000 sites—including MTFs, civilian providers, and comprehensive cancer centers—that offer cancer trials.

The agreement also allows all DoD MTFs and authorized TRICARE providers involved in oncology care to apply for participation in NCI clinical trial protocols for adult and pediatric cancers according to the usual NCI participation review process.

"Through this agreement, all TRICARE beneficiaries will have access to some of the most promising advances in cancer research through NCI-sponsored clinical trials throughout the country," added U.S. Army Major General Elder Granger, deputy director of the TRICARE Management Activity.

Retired Army Sergeant Major Michael Adams participated in the DoD-NCI demonstration project after he was diagnosed with advanced prostate cancer two years ago at age 47. "I had no knowledge of clinical trials before I was diagnosed and started searching the Internet," he explained. "When I searched the term 'clinical trials,' that ultimately led me to the TRICARE Web site which described the DoD-NCI demonstration project."

Sergeant Adams was referred to Memorial Sloan-Kettering Cancer Center where he entered a trial examining alternative methods of surgical anesthesia. "This program saved my life," he said. "When I first started in the program and came in to see the surgeon at Sloan-Kettering, he realized the severity of my diagnosis and literally cleared his schedule to make me his next patient."

He recalled: "I've never experienced such care in life, and I'm a combat vet who has had multiple surgeries in the past. I was treated at one of the world's leading cancer treatment centers. They are very supportive to patients and their families. They even spent time with my wife to explain my treatment and recovery, which is a very important part of my care."

Sergeant Adams is very pleased about TRICARE's decision to continue partnering with NCI. "I would highly recommend the program and clinical trial participation to other military personnel and their families," he said. ◆

Recently Seen in this Space

The NIH Public Access Policy will go into effect April 7. To read the recent Community Update article about the policy, go to http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_020508/page8. ◆