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Research results from the 'Era of Hope' Department of Defense breast cancer research program meeting

Second largest funder of breast cancer research to present cutting-edge results of studies on breast cancer

PHILADELPHIA, June 9, 2005 -- At the "Era of Hope" Department of Defense Breast Cancer Research Program meeting, researchers funded through this program will present innovative studies that offer a glimpse into the array of research currently being done on the prevention, detection, diagnosis and treatment of breast cancer. Studies presented at the meeting explore topics such as the development of a hand-held device to allow for at-home screening for breast cancer; the role of exercise in restoring the immune system after chemotherapy; and correlating genetic changes in normal-looking tissues near breast tumors with risk of recurrence.

Prototype Imager Holds Promise for At-home Breast Screening

A hand-held device in development may one day allow women to screen themselves for breast cancer in the privacy of their homes. The device, tentatively named "iFind," monitors the differences in blood oxygen ratios in growing cancers and normal tissues, reported researchers from the University of Pennsylvania. If it picks up potential early signs of breast cancer, it alerts the user with either a light or a vibration.

"It's important to know that this would be part of a breast exam, not a full diagnostic device," explained Britton Chance, Ph.D., emeritus professor of physics and radiology at

the University of Pennsylvania Medical School in Philadelphia, and developer of the device. "It would provide an indication of early signs of breast cancer that need to be followed up by a doctor."

The device measures oxygenation rather than blood volume to detect hypermetabolism -- the speedier growth rate of cancer cells. The prototype breast cancer detector performed with a positive predictive value of about 93%, which the researchers describe as a remarkably successful test for detecting breast cancer. Reliance on near-infrared light makes it a safe technology as well; women can use it as frequently as they wish. The study was conducted over a six-year period at two sites.

"This equipment gives women an opportunity to take charge of their own health, and it only requires minimal training," said Dr. Chance. "The device also has a longitudinal memory, so if something suspicious is flagged, the woman can bring the device with her to her doctor who will have results from every time it has been used."

In an informal, online survey of 325 women of all age groups and across all income levels conducted by the developers from a group of family, friends, acquaintances and others via word of mouth, 83% of respondents said they would be interested in a screening device they could use at home. Most of the women's concerns related to the reliability and sensitivity of the device and their ability to use it by themselves.

In addition to the hand-held imager, Dr. Chance is developing an imaging tool intended for use in a clinical setting rather than at home. The clinician's device produces crisp images with the aid of an injected molecular beacon called a nanodot -- a bright fluorescer that lights up tumors. Both devices would be able to detect small initial cancers as well as recurrences.

Initial studies have evaluated the hand-held device for principles of detection appropriate for breast cancer. Its developers propose to begin testing both imaging devices in a year and a half in an ongoing study of women with an identified BRCA 1 or 2 genetic defect, which places them at substantially greater risk for developing breast cancer.

Exercise Can Help Repair Chemotherapy-damaged Immune Systems in Breast Cancer Survivors

Exercise after chemotherapy for breast cancer boosted the activity of infection-fighting T cells in women who worked out regularly, according to data from a study conducted at Penn State. These findings indicate that exercise can help restore immune systems damaged by anti-cancer drugs, which destroy healthy as well as malignant cells.

Women between the ages of 29 and 71 were assigned to an exercise group (28 women) or a non-exercise group (21 women). In the intervention arm, women began the exercise routine usually within a month of completing post-surgical therapy. All exercisers followed a similar regimen ·stretching to warm up, use of Flexbands for resistance training, and an aerobic activity of their choice: treadmill, exercise bike, or walking. In the exercise group, each woman was paired with a kinesiology intern who served as a personal trainer.

"For the first three months, the women worked out with the trainers at our clinical research center three times a week for about 60 to 90 minutes, at a level the trainers determined was appropriate," said Andrea Mastro, Ph.D., professor of microbiology and cell biology at Penn State in University Park, PA. "We designed an exercise program that could be done without a gym so that during the second three months, participants had the option of working out at home."

Testing was conducted before the intervention, at three and six months. Measurements for some immune functions improved; exercisers showed more activated lymphocytes than non-exercisers. In addition, concentrations of IFN- α , an inflammatory substance that indicates trauma (e.g., from treatment), decreased in exercisers but increased in non-exercisers during the first three months. Another assay suggested that lymphocytes damaged or killed by therapy were replaced with new and responsive lymphocytes ·which divide to create more invader-fighting cells in response to foreign substances ·more quickly in exercisers.

"We know that chemotherapy-induced decreases in T cells can persist for many years, and data from the literature suggest that, in the period immediately following chemotherapy, the surviving T cells may be weakened as well," Dr. Mastro said. "That's why we're pleased to find evidence that appropriate exercise can help a breast cancer survivor's immune system bounce back after therapy." She noted that during the recruitment phase, some women said that their doctors had counseled them not to exercise after therapy.

Additional test results showed improvements in various physical functions such as endurance, upper-body strength (grip strength, biceps, triceps), and maximal oxygen intake (VO₂max). For women who exercised throughout the program, the physical function measures were better at six months than at three months. On a standard questionnaire, exercisers also scored higher on overall quality of life, social well-being, and experienced lower fatigue levels than the non-exercisers. There were no differences in results between women who exercised at home or at the research center.

Most exercisers preferred to continue with the personal trainers at the research center. Women who chose to work out at home kept an exercise log, which they discussed with the trainer during telephone interviews or weekly visits to the Penn State campus. During the first three months, compliance with the exercise regimen was about 82%, dropping to 76% during the second three-month period. According to feedback, distance from the university was a factor in the dropout rate.

There were no significant differences between the two groups in education, cancer treatment or stage, age, overall health, body mass index, or diet. In both groups, equal numbers of women had lumpectomy or mastectomy, most of the women had the same chemotherapy followed by radiation therapy, and most reported doing little if any regular exercise before diagnosis. Among those who had exercised before their diagnosis, walking was generally the activity of choice. The study excluded women who had other serious health conditions or took drugs that could affect the immune system.

Another study, conducted in a similar population by Canadian researchers and published in the April 2005 issue of the *Journal of Applied Physiology*, also found that exercisers had a greater percentage of activated T cells. Although that research was conducted for three months rather than six and examined aerobic conditioning rather than resistance training, Dr. Mastro considers the two studies complementary.

As a follow up, Dr. Mastro hopes to conduct a retrospective study of breast cancer survivors to determine whether their immune systems are still depressed five years after treatment.

Disease Recurrence Correlated with Genetic Changes in Normal-looking Tissue Near Breast Tumors

By identifying telltale genetic changes in breast tissues that appear normal, a new test may help predict the return of breast cancer after treatment, report researchers from

the University of New Mexico School of Medicine. The assay measures the DNA content of telomeres (TC), specialized nucleoprotein complexes that cap the ends of chromosomes, which are altered in tumors.

"We wanted to confirm that shortening of telomeres leads to genomic instability, which is a critical step in the progression to recurrent cancer," said Christopher Heaphy, a Ph.D. student in the department of biochemistry and molecular biology, University of New Mexico School of Medicine in Albuquerque, NM.

In previous studies, the group defined normal-length telomeres as having a TC value of 70% to 136% of a standard control. Telomeres with a TC value of less than 70% are considered tumor-like telomeres. Using mastectomy specimens from 11 women, the investigators examined tissue from the tumor at 1 cm and 5 cm distances from its visible edges. As expected, all 11 tumors had TC values of less than 70%. The assay the group developed also found tumor-like TC values in tissues that looked normal on standard laboratory analysis in nine of 11 tissues at the 1 cm point, and in zero at 5 cm. There was also an increase in allelic imbalance (AI), a reflection of genomic instability.

The researchers then examined samples from 25 women diagnosed with breast cancer around 1990 who were monitored on health status information after their mastectomies. The majority of tumors were large and had signs of spread to underarm lymph nodes. In addition to tumor specimens, they analyzed nearby tissue taken an unknown distance from the tumor margin. With the aid of long-term follow-up data on these women, Mr. Heaphy and his colleagues determined that tumor-like TC in normal-appearing tissues was associated with the return of breast cancer within 84 months of surgery. Specifically, TC values predicted relapse in seven of the 12 women whose breast cancer recurred.

In 12 of the 13 women who remained free of cancer, TC values of 70% or higher predicted this outcome. Earlier this year, the same research team published a paper showing that TC predicts outcome in prostate cancer.

"Our current TC assay is great for research labs, but it takes two days. We're now trying to develop a lower-cost, faster, and easier assay that will be practical in a clinical setting, to help identify women at high risk for disease progression," Mr. Heaphy said. "In roughly 30% of women with breast cancer, metastatic disease will develop even after

treatment. We believe that our TC assay can help identify these patients and allow the physician to make better informed decisions about further treatment."

The researchers also expect that their work showing genetic alterations in histologically normal breast tissue adjacent to the tumor will lead to a better definition of relevant surgical margins and a better assessment of risk of local recurrence after breast-conserving therapy.

In a much larger prospective project, the researchers are in the process of measuring TC and AI from tumors of 569 breast cancer survivors enrolled in the New Mexico Women's Health Study. This will allow the researchers to draw conclusions about the role of ethnicity in treatment, particularly in Hispanics, and whether TC can predict clinical outcome in a wider range of breast tumor types.

"Era of Hope" is a forum for the presentation of research supported by the U.S. Department of Defense's Breast Cancer Research Program (BCRP), an unprecedented partnership between the military, scientists, clinicians, and breast cancer survivors. Since 1992, the BCRP has been working to prevent and cure breast cancer by fostering new directions in research, addressing underserved populations and issues, encouraging the work of new and young scientists and inviting the voice of breast cancer survivors to be heard in all aspects of the program. One of many congressional research programs managed by the U.S. Army Medical Research and Materiel Command, the BCRP has received more than \$1.8 billion to date from Congress for innovative breast cancer research.

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"A New Approach to Early Detection for Women's Medicine"

B Chance, B Onaral, K Pour, M Herr

Embargoed Until: Thursday, June 9, 2:00 p.m.

"The Use of Exercise to Increase Lymphocyte Activation Following Chemotherapy for Breast Cancer"

A Mastro, N Hutnick, N Williams, W Kramer, R Dixon, A Bleznak

Embargoed Until: Thursday, June 9, 4:15 p.m.

"Telomere DNA Content and Allelic Imbalance in Histologically Normal Tissue Adjacent to Breast Tumors"

C Heaphy, M Bisoffi, C Fordyce, A Mangalik, J Griffith

Embargoed Until: Thursday, June 9, 6:30 p.m.
