SOUTHWESTERN NEWS

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GENETIC TESTING, COMPUTER RISK-ASSESSMENT SOFTWARE PROVE EFFECTIVE IN PREDICTING BREAST CANCER

DALLAS – June 5, 2002 – Researchers at UT Southwestern Medical Center at Dallas have shown that examining breast cells' molecular makeup can provide a better way to predict breast-cancer risk and that computer-based risk-assessment tools can help identify women who would benefit from genetic testing.

The findings are published in separate papers in today's edition of the *Journal of the National Cancer Institute*. Dr. David Euhus, associate professor of surgical oncology, is the lead author on both papers. He said that while the studies were separate, both suggest new approaches for identifying women at increased risk for breast cancer.

The women participating in the cell-examination study were not cancer patients; however, their risk of developing breast cancer had been assigned as low, moderate or high using the Gail model. The Gail model is a computer model known to be an accurate predictor of women's risk of developing breast cancer. Euhus found that the detection of small DNA deletions in breast cells from these women correlated with Gail-model risk and with precancerous changes in the cells diagnosed by routine microscopy.

"Our findings suggest that it is possible to develop an individualized approach to risk assessment using breast cells obtained by various methods," Euhus said.

While the Gail method is accurate at assigning risk, it can't predict which women it rates as high risk actually will develop breast cancer. Molecular analysis of breast cells may solve this problem.

In the cell-examination study, Euhus and his colleagues obtained cell samples from the breast through fine-needle aspiration, using a small-gauge needle to extract clusters of cells. Euhus said cells also could be gathered for analysis using methods such as ductal lavage, where cells are collected from milk ducts.

In addition to traditional microscopic examination for outward abnormalities, the cells were subjected to DNA analysis to look for internal damage that could foreshadow the genetic mutations that cause breast cancer. Some cells that showed no outward irregularities were found to have DNA damage.

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"We know that the genome becomes unstable before the cancer forms," Euhus said. "For whatever reason, certain cells in an organ stop making accurate copies of their DNA when they divide, and they don't fix DNA damage like they should."

The second study compared the effectiveness of experienced genetic counselors at identifying *BRCA* mutation carriers against that of BRCAPRO, a statistics-based software tool. Euhus, who developed a BRCAPRO interface for his own CancerGene risk-assessment package, said the software did just as well as experienced counselors at identifying mutation carriers.

That's important, he said, because such analysis is a vital step. Some women at very high risk may opt for preventive surgical removal of their breasts or ovaries and fallopian tubes before cancer can form. Such surgeries dramatically reduce cancer risk, but the decision is difficult to make. Euhus said the results show that BRCAPRO and possibly other automated tools could complement experienced genetic counselors and help less-experienced counselors make recommendations.

"Of the women with a family history of breast cancer, we need to know which ones to send on for genetic testing. This will identify the highest-risk women who are likely to benefit from preventive surgery," he said.

Other UT Southwestern contributors to the cell-examination study were Dr. George Peters, executive director of the Southwestern Center for Breast Care; Dr. A. Marilyn Leitch, medical director of the Southwestern Center for Breast Care; and Dr. Adi F. Gazdar, senior author of the paper and professor of pathology in the Nancy B. and Jake L. Hamon Center for Therapeutic Oncology Research.

UT Southwestern collaborators on the study comparing the effectiveness of BRCAPRO with genetic counselors were Linda Robinson, a genetic counselor in the Harold C. Simmons Comprehensive Cancer Center; and Dr. Gail Tomlinson, senior author and director of the Mary L. Brown Breast Cancer Genetic Risk Assessment Program. Other institutions contributing to the study were the University of Chicago; the Dana-Farber Cancer Institute, Boston; UT M.D. Anderson Cancer Center; the University of California, San Francisco, School of Medicine; Massachusetts General Hospital; the University of California, Los Angeles, School of Medicine; and the University of Kansas Medical Center.