

SOUTHWESTERN NEWS

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EMBARGOED UNTIL 4 P.M. CDT MONDAY, JUNE 7, 2004

UT Southwestern researchers develop blood test that can detect genetic changes in progressive breast cancer

DALLAS – June 7, 2004 – Researchers at UT Southwestern Medical Center at Dallas have developed a blood test that can detect amplification of a certain gene found in circulating cells associated with breast cancer.

If further clinical studies bear out its effectiveness, researchers say the blood test could be used as a standard operating procedure to monitor genetic changes for which a treatment is available.

“Cancer is a moving target, and the oncologist has to know which bullet to put in his gun,” said Dr. Jonathan Uhr, professor of microbiology and internal medicine in the Cancer Immunobiology Center at UT Southwestern and senior author of the study. “Obtaining repeated blood samples is a safe and routine procedure, and this test can help the oncologist determine whether a new genetic change has become dominant and calls for a specific treatment for that change.”

Their work will appear in an upcoming issue of the *Proceedings of the National Academy of Sciences* and is currently available online.

The researchers developed a blood test to optimize the detection and characterization of circulating cancer cells shed from a primary tumor. This is done by matching the cells’ genetic abnormalities with the parent tumor.

The test can detect one circulating tumor cell in 10 million white blood cells, said Dr. Uhr.

The research augments previous work by UT Southwestern researchers to determine if patients whose primary tumor did not have amplification of the gene *HER-2* could acquire amplification if the tumor recurred and progressed. Using the new blood test to examine the circulating tumor cells from growing tumors, initial indications are this amplification eventually can occur, Dr. Uhr said.

Dr. Uhr says that in a patient whose primary tumor is classified as *HER-2* gene non-amplified, a minute number of tumor cells actually may be *HER-2* amplified. With time and selective pressures, this small population expands and becomes the predominant one.

Overexpression of the *HER-2* gene occurs in about 20 percent to 25 percent of breast-cancer patients. Prognosis is poor, as the cancer cells often resist radiation therapy and almost all drugs.

However, studies have shown that the drug Herceptin (an antibody to *HER-2*) can treat tumors with *HER-2* amplification by itself in 25 percent of patients and in 50 percent when combined with

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chemotherapy. The antibody binds to the molecules that are produced by the *HER-2* gene and reside on the cancer cells' surface. The drug neutralizes their effect with far fewer side effects than conventional chemotherapy.

By utilizing this blood test to determine *HER-2* gene amplification in circulating cancer cells, doctors may be able to provide Herceptin to certain patients who have acquired such amplification. At present, *HER-2* amplification is only diagnosed in the primary tumor.

“The implications of tumor evolution over the course of treatment are significant,” said Dr. Debasish Tripathy, professor of internal medicine and contributing author. “A better understanding of this process will not only allow us to use available drugs in a more individualized fashion but also may point to new therapeutic approaches.” Dr. Tripathy heads the Komen/UT Southwestern Breast Cancer Research Program.

The next step is to evaluate patients whose circulating tumor cells have acquired *HER-2* gene amplification to determine if these cells are reflecting the genetic status of the recurrent tumor, said Dr. Uhr. For the blood test to be considered worthwhile, research also must show that therapy with Herceptin alone or in addition to a chemotherapeutic agent can cause remissions in a significant number of patients.

Other UT Southwestern contributors to the *PNAS* study were Dr. Raheela Ashfaq, professor of pathology; Dr. Eugene Frenkel, professor of internal medicine; Dr. Marilyn Leitch, professor of surgical oncology; Dr. David Euhus, associate professor of surgical oncology; Dr. Barbara Haley, associate professor of internal medicine; Dr. Cynthia Osborne, assistant professor of internal medicine; Dr. Susan Hoover, assistant professor of surgical oncology; Dr. Edward Clifford, clinical assistant professor of surgery; and in the Cancer Immunobiology Center, Dr. Ellen Vitetta, director; Dr. Songdong Meng, postdoctoral researcher; Dr. Jianqiang Wang, postdoctoral researcher; Thomas Tucker, senior research scientist; and Nancy Lane, research scientist.

Researchers from UT M.D. Anderson Cancer Center; Texas Oncology PA; Dallas Surgical Group; Cancer Center Associates in Dallas; Vysis, Inc.; Wistar Institute; Immunicon Corp.; the Washington University School of Medicine in St. Louis; and Germany's University of Tubingen also contributed.

Research was supported by the Raymond D. Nasher Cancer Research Program and the Komen/UT Southwestern Breast Cancer Research Program.

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