DEUTSCHES KREBSFORSCHUNGSZENTRUM IN DER HELMHOLTZ-GEMEINSCHAFT

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Gene Profile to Help Decide on Breast Cancer Treatment

In 25 to 30 percent of breast cancer patients, tumors regress completely under chemotherapy. For sufferers and clinicians alike it would be helpful to have indicators showing in advance who will profit from this often stressful treatment. Scientists of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) and the University Women's Hospital in Heidelberg have now identified a specific gene activity profile which characterizes those tumors that respond by complete regression to a special treatment regimen.

In breast cancer patients, complete tumor regression in the course of chemotherapy is a favorable prognostic factor. If the treatment is started prior to surgical removal of the tumor, doctors can also observe whether the tumor responds by regression as hoped for. However, not all patients benefit equally from chemotherapy: Depending on the treatment regimen, no more tumor cells are found in tissue examinations of 25 to 30 percent of patients after completion of the prescribed treatment cycles. The remaining sufferers do not or only partially respond to the drugs.

An innovative chemotherapy regimen for breast cancer is a combination of gemcitabine, docetaxel and epirubicin. Clinicians and scientists of the German Cancer Research Center and the Heidelberg University Women's Hospital have developed a test to predict in which patients this drug combination will lead to a complete elimination of tumor cells in the breast. The test is performed using biopsy material obtained from cancerous knots. One hundred breast cancer patients whose tumors had not yet started metastasizing were included in the study.

Using a gene chip representing 21.139 human genes, the researchers identified a specific pattern of gene activities in the cancer cells of a group of patients. This activity profile is characteristic of those tumors that are completely eliminated by the triple therapy. In a second group of affected women, the scientists subsequently showed that the success of a triple therapy can be predicted using this activity pattern.

The activity (expression) pattern, also called "signature", of chemotherapy-sensitive tumors encompasses 512 different genes. Most of these carry information for proteins that are involved in DNA repair or programmed cell death (apoptosis) or that regulate the activity of other genes.

"A crucial factor determining the prognostic value of our test is the fact that we have not simply studied the response to the triple therapy. Instead, we have concentrated on complete tumor regression. Thus, we increase the significance of the test," says Professor Peter Lichter of the German Cancer Research Center. "Whether and when the test can be used in clinical practice will now be determined in studies with larger groups of patients."

With 55.000 newly diagnosed cases each year, breast cancer is the most frequent cancer in women in Germany. In 2003, 17.173 women died of breast cancer. About 79 percent of patients survive the first five years after diagnosis.

Publication: Gene Expression Signature Predicting Pathologic Complete Response to Primary Systemic Chemotherapy With Gemcitabine, Epirubicin and Docetaxel in Primary Breast Cancer.Olaf Thuerigen, Andreas Schneeweiss, Grischa Toedt, Patrick Warnat, Meinhard Hahn, Heidi Kramer, Benedikt Brors, Christian Rudlowski, Axel Benner, Florian Schuetz, Bjoern Tews, Roland Eils, Hans-Peter Sinn, Christof Sohn and Peter Lichter, Journal of Clinical Oncology, Vol. 24, No. 12, 20 April 2006

The task of the Deutsches Krebsforschungszentrum in Heidelberg (German Cancer Research Center, DKFZ) is to systematically investigate the mechanisms of cancer development and to identify cancer risk factors. The results of this basic research are expected to lead to new approaches in the prevention, diagnosis and treatment of cancer. The Center is financed to 90 percent by the Federal Ministry of Education and Research and to 10 percent by the State of Baden-Wuerttemberg. It is a member of the Helmholtz Association of National Research Centers (Helmholtz-Gemeinschaft Deutscher Forschungszentren e.V., HGF).

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Dr. Julia Rautenstrauch
Presse- und Öffentlichkeitsarbeit
Deutsches Krebsforschungszentrum
Im Neuenheimer Feld 280
D-69120 Heidelberg
T: +49 6221 42 2854
F: +49 6221 42 2968