GERMAN CANCER RESEARCH CENTER
IN THE HELMHOLTZ ASSOCIATION

No. 2 February 2, 2004 (And)

Leukemia: Towards individually customized therapy

Gene analysis using chip technology helps doctors choose the right treatment

Disease progression in patients suffering from B-cell chronic lymphocytic leukemia can vary considerably. For physicians treating these patients the prognosis of disease progression is an important criterion for the choice of therapy. Typical genetic changes in the tumor cells serve as an indicator of the prognosis. Thus, in clinical practice it is helpful to screen for the respective chromosome defects. A valuable tool to use in this search is a chip developed at the Deutsches Krebsforschungszentrum (German Cancer Research Center, Heidelberg) in collaboration with scientists of the universities of Heidelberg and Ulm. In the latest issue of the science journal Proceedings of the National Academy of Sciences of the USA (PNAS)*, the research team of Carsten Schwänen and Peter Lichter describe how typical defects in the genetic material of leukemia cells can be identified using the chip tool.

Like other malignant tumors, leukemias often display typical changes in the genome, i.e., chromosome fragments are either lost or gained. Several typical gene defects of B-CLL tumor cells are already known. The research group headed by Hartmut Döhner of Ulm University were able to show that a loss of genetic material in chromosomes 11 and 17 are associated with a poor prognosis. Based on these findings Schwänen and his colleagues have developed a chip that facilitates large-scale comparisons of the genetic material (DNA) of leukemia cells and healthy cells. This method is called matrix-based comparative genomic hybridization, or matrix CGH for short. In a single matrix CGH assay it is possible to identify several thousand different gains and losses of DNA in the genome of a tumor cell at the same time. What makes this test system special is the fact that it is very sensitive to the typical chromosome aberrations and detects these with high reliability. Moreover, the analysis does not take much time and effort – ideal prerequisites for clinical use. The researchers tested the validity of the results obtained using the newly developed chip with the aid of a related, but more complicated method called fluorescence in situ hybridization (FISH), which is used to detect chromosome changes in intact cells. The results speak for themselves: The DNA losses and gains detected corresponded 100 percent in both analysis methods. As another achievement the genome researchers discovered another two changes in the genetic material that seem to be typical of B-CLL: amplification of the MYCN oncogene and triplication of chromosome 19. The latter appears to be associated with a more favorable disease progression.

The high reliability of characterization of leukemia cells and the uncomplicated handling make the chip a promising tool aiding in treatment decisions. But the chip has yet to pass the practical test. It will be utilized in clinical studies to determine whether a patient suffering from B-CLL with a specific chromosome change is treatable by less aggressive chemotherapy or whether the doctors need to consider a stem cell transplant, which promises better chances of recovery but involves much higher risks.

*Carsten Schwänen et al., PNAS, January 27, 2004, vol. 101, no. 4,

1039-1044.

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.).

This press release is available at www.dkfz.de/pressemitteilungen

Dr. Julia Rautenstrauch
Division of Press and Public Relations
Deutsches Krebsforschungszentrum
Im Neuenheimer Feld 280
D-69120 Heidelberg
T: +49 6221 42 2854
F: +49 6221 42 2968