

Childhood Brain Tumors: Molecular Marker to Facilitate Prognosis and Treatment Planning

Valuable results for the complex jigsaw puzzle of cancer development

CDK6 is the plain name of a molecule that is often characteristically altered in medulloblastoma. This type of cancer is among the most common malignant brain tumors in children. Heidelberg molecular geneticists of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) have now found out that CDK6 can serve as an important indicator to help physicians determine the prognosis of patients. The results obtained in a project of the National Genome Research Network within the Brain Tumor Network have been published in the latest issue of the *Journal of Clinical Oncology**

The typical age at the onset of medulloblastoma is seven years. Frequently, the tumor has already spread to other parts of the body. Despite intensive treatment almost half of the young patients die of this cancer. To be able to evaluate the course of such a tumor disease based on characteristic molecular markers and to develop novel treatment strategies, cancer researchers are trying to elucidate the development of the disease.

Frank Mendrzyk and Dr. Bernhard Radlwimmer of the Molecular Genetics Division have now contributed an important puzzle piece. The two researchers used the matrix-CGH technology developed by their divisional head Professor Peter Lichter to identify genetic alterations in medulloblastoma. Working with tissue samples of brain tumors they started by searching the whole genome for overrepresented and underrepresented segments of genetic material. Then they used immunological detection methods to investigate how identified candidate genes of these regions and their products are interconnected with the stage and course of the disease. This study was based on tumor tissue obtained from more than 200 patients whose medical records are known. The investigators found out that an increased number of gene copies is associated with overproduction of CDK6 and an unfavorable course of the disease. The gene located on chromosome 7 appears to play a key role in signaling pathways influencing growth and differentiation of medulloblastoma cells and other tumor cells. Compared to previously available markers, CDK6 seems to be an independent and at the same time more reliable source of information. Moreover, the gene product is easy to detect with immunological methods that are already established in routine diagnostics. CDK6 is also useful in clinical trials when it comes to evaluating the response to a treatment strategy.

The molecular geneticists have even more valuable findings to present. A factor called PPM1D is typically overproduced in medulloblastoma due to amplification of DNA segments on chromosome 17. The gene is not unknown to scientists. It is also found in multiple copies in neuroblastoma as well as in breast and ovarian cancer. Earlier publications have presented evidence suggesting that these alterations of the genetic information play a role in cancer development. Thus, other scientists showed in mouse embryonic cells that PPM1D is capable of abrogating the function of tumor suppressor gene TP53. TP53, jointly with other genes, regulates cell multiplication and thus reduces the likelihood of a cell turning into a tumor cell. Conversely, cells were resistant to transformation when they lacked PPM1D.

Further analyses and functional studies need to be performed in order to understand the exact role these genes play in the development of medulloblastoma. Eventually, cancer researchers are hoping to use this knowledge to find new targets for therapies and thus positively influence the course of the disease.

* Frank Mendrzyk, Bernhard Radlwimmer et al.: "Genomic and protein expression profiling identifies CDK6 as novel independent prognostic marker in medulloblastoma", Journal of Clinical Oncology, Dec 1, 2005; 23 (34)

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

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