

New classification for malignant brain tumors

Based on a combination of molecular-biological data with clinical parameters, it is possible to classify glioblastoma, the most malignant type of brain tumor, into six subgroups. An international research team led by molecular biologists from the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) has now reported these results of a study, which was the first to comprise tumors of patients of all age groups. The molecular fingerprints of the individual tumor groups may help to develop differentiated treatments and to plan clinical trials more specifically.

Glioblastomas grow extremely aggressively into healthy brain tissue and, moreover, are highly resistant to radiation therapy and chemotherapy. Therefore, they are regarded as the most malignant type of brain tumor. Currently available treatment methods are frequently not very effective against this type of cancer. Glioblastoma can affect people of all ages, but is less common in children than in adults. In Germany, about 6,000 people are newly diagnosed with this type of tumor each year.

“Based on our latest results, we should rather say that they are affected by one of this group of tumors,” says Prof. Dr. Stefan Pfister, a molecular biologist who is head of a research department at DKFZ and also works as a pediatrician in the Department of Pediatric Oncology of Heidelberg University Hospitals. He has now led a team of molecular geneticists from numerous universities in Germany, the U.S.A. and Canada in a project to analyze and classify the genomes of 210 glioblastoma patients of all age groups.

The investigators focused on mutations in the DNA sequence, the activity pattern of all genes, deletions and duplications of DNA. In addition, they studied the pattern of what are called methyl tags, a type of tiny chemical attachments to the DNA bases, which are summarized by scientists under the term of “epigenetic changes”. In combination with clinical data such as age at onset of disease, life expectancy, and anatomical location of the tumor, these parameters enabled the researchers to define six distinct subgroups of glioblastoma.

“We have been the first to comprise tumors of patients of all age groups in one study,” says Dominik Sturm, who is among the study’s first authors. “This made it possible for us to recognize, for example, that adult patients are also occasionally affected by tumors which we had believed to be characteristic of childhood cancers.”

Early this year, Pfister’s group had already discovered two different mutations in the gene for a type of DNA packaging protein in pediatric glioblastoma. “Although they affect one and the same gene, these two mutations now define two of our six tumor groups which differ substantially from each other. They even occur in different areas of the brain,” said Sturm.

“The precise knowledge of the different molecular backgrounds of glioblastoma may be the compass that will lead us to novel treatment approaches which are customized for one of the subgroups,” says Stefan Pfister. For example, two of the newly defined groups are characterized by strongly diverging patterns of epigenetic tags. “It is possible that our results may rapidly lead to clinical applications, because we already have drugs available that act on epigenetic tags,” the pediatrician explains. Moreover, clinical trials can better be planned and evaluated if the individual tumor groups are considered separately.

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The German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) with its more than 2,500 employees is the largest biomedical research institute in Germany. At DKFZ, more than 1,000 scientists investigate how cancer develops, identify cancer risk factors and endeavor to find new strategies to prevent people from getting cancer. They develop novel approaches to make tumor diagnosis more precise and treatment of cancer patients more successful. Jointly with Heidelberg University Hospital, DKFZ has established the National Center for Tumor Diseases (NCT) Heidelberg where promising approaches from cancer research are translated into the clinic. The staff of the Cancer Information Service (KID) offers information about the widespread disease of cancer for patients, their families, and the general public. The center is a member of the Helmholtz Association of National Research Centers. Ninety percent of its funding comes from the German Federal Ministry of Education and Research and the remaining ten percent from the State of Baden-Württemberg.

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