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Precision Diagnosis of Brain Tumors: Antibody to Detect Enzyme Defect

More than 100 different types of brain tumor are known in medicine. Their exact diagnosis is often difficult, because only tiny amounts of tumor tissue are usually available. Scientists of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) and the University of Heidelberg have developed an antibody which is highly specific for the characteristic alteration of an enzyme that is typical of two dangerous types of brain tumor. The antibody promises to make diagnosis easier and more exact and also allows making a prognosis of disease progression.

Tumors of the adult brain are a comparatively rare, but particularly dreaded disease which often dramatically changes the lives of those affected. There are different types of brain tumor depending on the tissue from which they originate. The term ‘glioma’ refers to a group of malignant brain tumors that arise from glial cells, which support and nourish the brain. Gliomas constitute approximately 20 percent of brain tumors. Two common types of glioma are astrocytomas and oligodendrogliomas.

When there is a suspicion of a brain tumor, the diagnostic procedure usually starts with a type of imaging technology such as an MRI scan. The result subsequently needs to be confirmed by a neuropathologist using a tissue sample of the tumor. In order to start specific treatment, it is important to obtain an exact diagnosis of the type of tumor. This is where neuropathologists sometimes reach their limits: “We often get tissue from the outer zone of a tumor where we usually do not find the typical textbook picture,” says Andreas von Deimling, head of the Clinical Cooperation Unit “Neuropathology”, which is based at DKFZ and the Institute of Pathology of Heidelberg University. Additional difficulties for the pathologists arise from the fact that they have to examine tiny samples and the tissue is often deformed when taken out.

Therefore, von Deimling and his co-workers were looking for a tool that would make first diagnosis and differentiation of brain tumors easier and more secure. Almost 70 percent of astrocytomas and oligodendrogliomas carry a mutation in the gene coding for the enzyme IDH1 (isocitrate dehydrogenase). Ninety percent of IDH1 mutations are located in exactly the same amino acid building block at position 132 of the enzyme. Jointly with antibody specialist Professor Hanswalter Zentgraf and his co-workers from DKFZ, the neuroscientists were able to develop a monoclonal antibody which can only attach to the IDH1 enzyme if the mutation is present at position 132. The antibody does not bind to the unaltered enzyme.

The antibody fulfills another key requirement for use in clinical routine: It also reacts with paraffin embedded tissue sections. Thus, if the antibody reaction is positive, pathologists will now be able to obtain a secure diagnosis of astrocytoma or oligodendrogliomas even in difficult sample material. Moreover, they were able to detect individual cancer cells in the tissue zone around the tumor.

Andreas von Deimling expects that the antibody, for which a patent application is filed, will be used in brain tumor diagnostics worldwide. Furthermore, researchers have recently found out, jointly with Wolfgang Wick, head of the Clinical Cooperation Unit “Neurooncology” at DKFZ, that mutations in the IDH1 enzyme of astrocytomas and oligodendrogliomas are correlated with a favorable prognosis of disease progression. Further studies will now determine whether this may lead to corresponding therapy adjustments. Above all,

neuropathologist von Deimling is sure that the antibody will play a key role in his further research: “Now we want to find out whether and how IDH1 mutations are involved in the development of cancer in the brain,” he said.

David Capper, Hanswalter Zentgraf, Jörg Balss, Christian Hartmann, Andreas von Deimling: Monoclonal antibody specific for IDH1 R132H mutation
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Contact:
Dr. Stefanie Seltmann
Presse- und Öffentlichkeitsarbeit
Deutsches Krebsforschungszentrum
Im Neuenheimer Feld 280
D-69120 Heidelberg
T: +49 6221 42 2854
F: +49 6221 42 2968