

Plant Pathogen Yields Substance to Fight Neuroblastoma

Drug treatment of neuroblastoma, a tumor of the nervous system in children, poses major problems. Therefore, scientists at the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) have been searching for substances that are suitable as a basis for developing better drugs. Now they have found a candidate: HC-toxin, which is isolated from a fungal plant pathogen. The substance from the maize pathogen reprograms neuroblastoma cells in such a way that they behave almost like healthy cells again.

Normally, the fungus *Helminthosporium carbonum* leads to reduced harvests for maize farmers. Yet a specific constituent of the pathogen, namely HC-toxin, might be very useful for medicine. The substance is used by scientists as a basis for developing a new anti-cancer drug. HC-toxin acts on enzymes known as histone deacetylases (HDACs), which structure the packaging of the genetic material, or DNA. HDAC enzymes change, among others, the histones – proteins around which the DNA is wrapped. Alterations in the packaging of the genetic material are suspected to cause cancer or promote its spread. Therefore, scientists are studying substances that inhibit HDAC enzymes for their ability to fight malignant tumors. Among these substances is HC-toxin, which has now been investigated by researchers of the Clinical Cooperation Unit “Pediatric Oncology” at the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ). They found out that neuroblastoma cells lose several of their cancer-typical properties when under the influence of the substance: They divide less frequently, show less invasive growth and even their outside appearance resembles healthy nerve cells again. These effects were observed to be stronger than with other HDAC inhibitors investigated previously.

The effect of HC-toxin is presumably based, among other things, on the fact that it promotes the function of an important cellular “cancer brake” known as RB signaling pathway. The investigators found out that the cancer brake was much more active in tumors cells that had been treated with HC-toxin than in untreated cells. They plan to conduct further research to determine whether the substance derived from the maize pathogen is suitable for developing a new drug to fight neuroblastoma.

Neuroblastoma is the second most frequent malignant tumor in children. With an average of 150 new cases diagnosed in Germany each year, neuroblastoma constitutes about seven to eight percent of all childhood cancers. Most affected children are in preschool age, one third are diagnosed under one year of age. Although treatment has been improved over the past few years, chances of recovery from advanced stage neuroblastoma continue to be very low. In addition, the drugs being used often cause serious side effects.

Hedwig E. Deubzer, Volker Ehemann, Frank Westermann, Ralf Heinrich, Gunhild Mechttersheimer, Andreas E. Kulozik, Manfred Schwab, Olaf Witt. Histone deacetylase inhibitor *Helminthosporium carbonum* (HC)-toxin suppresses the malignant phenotype of neuroblastoma cells. *International Journal of Cancer*, DOI: 10.1002/ijc23295

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.).

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