

Drug activates virus against cancer

Scientists from the German Cancer Research Center (DKFZ) have discovered that a drug called valproic acid increases the effectiveness of parvoviruses that are used against cancer. In some cases, pancreatic and cervical tumors that had been transplanted to rats completely regressed after treatment with a combination of the virus and an agent. The drug makes the viruses replicate more rapidly and improves their capacity to kill cancer cells.

Parvoviruses cause no harm in humans, but they can attack and kill cancer cells. Since 1992, scientists at the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) have been studying these viruses with the aim of developing a viral therapy to treat glioblastomas, a type of aggressively growing brain cancer. A clinical trial has been conducted since 2011 at the Heidelberg University Neurosurgery Hospital to test the safety of treating cancer patients with the parvovirus H-1.

“We obtained impressive results in preclinical trials with parvovirus H-1 in brain tumors,” says Dr. Antonio Marchini, a virologist at DKFZ. “However, the oncolytic effect of the viruses is weaker in other cancers. Therefore, we are searching for ways to increase the therapeutic potential of the viruses.”

In doing so, the virologists also tested valproic acid, a drug belonging to a group of drugs called HDAC inhibitors. The effect of these inhibitors is to raise the transcription of many genes that have been chemically silenced. Valproic acid is commonly used to treat epilepsy and has also proven effective in treating specific types of cancer.

The researchers initially used a combination of parvoviruses and valproic acid to treat tumor cells that had been obtained from cervical and pancreatic carcinomas and raised in the culture dish. In both types of cancer, the drug raised the rate of virus-induced cell death; in some cases, the cancer cells were even completely eliminated.

The encouraging results obtained in cultured cells were confirmed in cervical and pancreatic tumors that had been transplanted to rats. After the animals were treated with a combination of parvoviruses and valproic acid, in some cases the tumors regressed completely and animals remained free of recurrences over a one-year period. In contrast, animals treated with the same virus dose without the drug displayed no regression, not even when a 20-times higher dose of viruses was administered.

The virologists were also able to unravel the molecular mechanism by which valproic acid assists parvoviruses in fighting cancer: Treatment with the drug activates a viral protein called NS1, which is toxic. This helps the viruses replicate more rapidly and kill cancer cells more effectively.

“The synergistic effect of a combination of parvoviruses and valproic acid enables us to deliver both the viruses and the drug at low doses, which prevents severe side effects,” Marchini explains. “The results are encouraging us to carry out further tests of this combination therapy. We believe it has the potential to arrest tumor growth in severe cases of cancer.”

Junwei Li, Serena Bonifati, Georgi Hristov, Tiina Marttila, Severine Valmary-Degano, Sven Stanzel, Martina Schnölzer, Christiane Mougin, Marc Aprahamian, Svitlana P. Grekova, Zahari Raykov, Jean Rommelaere and Antonio Marchini: Synergistic combination of valproic acid and oncolytic parvovirus H-1PV as a potential therapy against cervical and pancreatic carcinomas. EMBO Molecular Medicine 2013, DOI: 10.1002/emmm.201302796

A picture for this press release is available at:

<http://www.dkfz.de/de/presse/pressemitteilungen/2013/images/redVirus.jpg>

Caption: Computer-generated representation of parvovirus H-1, Antonio Marchini, German Cancer Research Center (DKFZ)

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. The staff of the Cancer Information Service (KID) offers information about the widespread disease of cancer for patients, their families, and the general public. 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. In the German Consortium for Translational Cancer Research (DKTK), one of six German Centers for Health Research, DKFZ maintains translational centers at seven university partnering sites. Combining excellent university hospitals with high-profile research at a Helmholtz Center is an important contribution to improving the chances of cancer patients. DKFZ is a member of the Helmholtz Association of National Research Centers, with ninety percent of its funding coming from the German Federal Ministry of Education and Research and the remaining ten percent from the State of Baden-Württemberg.

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