Viruses against cancer

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Advanced gliomas regressed completely in rats after treatment with parvoviruses and the animals survived significantly longer than untreated animals. This was shown by scientists of the German Cancer Research Center.

Particular parvoviruses normally infect rodents, but they are also infectious for human cells. However, they do not cause any disease symptoms in humans. Most importantly, these viruses have an astonishing property: They kill infected tumors cells without causing any damage to healthy tissue. Therefore, scientists in the teams of Jean Rommelaere and Jörg Schlehofer at the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) have been investigating over the past years whether these viruses can be used as weapons against cancer.

Many different viruses have been tested before in cancer therapy, particularly for treating those types of cancer for which there are no effective established treatment methods. The DKFZ researchers realized early on that parvovirus H-1 has important advantages over other viruses. Now they have been the first to prove that malignant glioblastomas regress completely as a result of treatment with these viruses.

The treatment experiments were conducted in rats who had received brain tumors cells by implantation. Once the resulting brain tumors had reached a specified size, the animals were given parvoviruses, either by direct injection into the tumor or via the blood stream. In those animals in which the viruses had been injected directly into the tumor, the

tumors shrank visibly after only three days and even disappeared completely in eight of twelve animals treated. The rodents survived without any symptoms, while untreated control animals suffered from severe disease symptoms within three weeks following tumor cell implantation. In the intravenously treated group, tumors regressed completely in six of nine animals. The animals have survived for more than one year now without any symptoms or late side effects of therapy.

The researchers found no infection-related damage in the nervous tissue surrounding the tumor. The viruses did not spread to the whole organism. Although parvovirus DNA was detectable in all organs after several days following virus transfer, this was only for a short time. The viruses had infected healthy cells, but these did not produce a new virus generation. However, in the tumor tissue, the viruses reproduced and viral protein production was detected only in these cells. In rats that did not bear tumors, the viruses did not reproduce. Thus, it appears that the presence of cancer cells is a necessary condition for the parvoviruses to reproduce.

After the positive results of these experiments the DKFZ researchers are convinced that parvoviruses are suitable candidates for use in cancer treatment. Professor Jean Rommelaere summarizes the reasons why: "Parvovirus H-1 does not cause any disease symptoms in humans. Since we are normally not immune against rodent viruses, it is not immediately eliminated by the human immune system after injection. Parvoviruses kill tumors due to natural properties so that their genetic material does not need to be genetically manipulated like herpes viruses, polio viruses or adenoviruses, which have been used in other studies. Moreover, they do not incorporate their genetic material into the host cell's genome, so we need not fear that they might 'accidentally' boost growth-promoting genes."

Rommelaere's colleague, Jörg Schlehofer, adds two more qualities that

could be decisive for therapy of glioblastomas, in particular: "Parvoviruses pass the blood brain barrier so that they can be administered via the blood stream. In addition, they reproduce in cancer cells, which is particularly important for successful treatment of glioblastoma with its diffuse growth. Thus, the second generation viruses reach and eliminate even those cancer cells that have already settled at some distance from the primary tumor."

Parvovirus therapy to be tested in clinical trial

The promising results in the animal model have encouraged the DKFZ scientists, jointly with Dr. Karsten Geletneky of the Neurosurgery Department of Heidelberg University, to plan a clinical trial on the treatment of advanced glioblastomas. Glioblastoma is considered the most threatening type of brain tumor; only about half of those affected survive the first year after diagnosis. Even innovative drugs that have been made available recently can prolong survival only marginally. Therefore, new treatment approaches for this type of cancer are urgently needed.

Preparing such a trial is a tremendous effort. Thus, large amounts of virus have to be produced under controlled conditions for toxicological tests. Therefore, even a large institute like DKFZ could not afford financing a transfer of these results into clinical practice. Continuation of viral therapy development was made possible only by funds from Munich-based company Oryx. The company aims to provide funds for the development of therapeutically effective substances into clinically applicable drugs in an early stage.

Many of the required toxicological data have already been obtained and submitted to the drug approval authority by the researchers so that they expect to be able to admit the first patients to the trial by the end of the year. In addition, DKFZ and Oryx have recently signed another

agreement: Oryx will also get involved in the development of a parvovirus therapy against pancreatic cancer.

More information: Karsten Geletneky, Irina Kiprianova, Ali Ayache, Regina Koch, Marta Herrero y Calle, Laurent Deleu, Clemens Sommer, Nadja Thomas, Jean Rommelaere and Jörg R. Schlehofer: Regression of advanced rat and human gliomas by local or systemic treatment with oncolytic parvovirus H-1 in rat models. Neuro-Oncology 2010, DOI: 10.1093/neuonc/noq023

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