

Using Viruses to Fight Brain Tumors Bridging the Gap Between Research and Clinical Application

Parvoviruses can enter and kill cancer cells, but they do not cause disease in humans. 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 against dangerous brain tumors that are almost impossible to treat. This week, the first ever phase I/IIa clinical trial will start at the Neurosurgery Department of Heidelberg University Hospital to test the safety of parvovirus therapy. Developing this innovative treatment method to the stage of clinical application has been made possible in collaboration with Oryx GmbH & Co KG.

Since 1992, Professor Jean Rommelaere of DKFZ has been investigating the oncolytic (cancer-killing) properties of parvoviruses. These viruses of only 20 nanometers in diameter are among the tiniest of all known viruses. Parvoviruses, which replicate exclusively in dividing cells, do not cause any serious symptoms in humans. Moreover, they do not insert their DNA into the genome of infected cells so that there is no risk of activating growth-promoting genes.

For his work, Rommelaere chose H1 parvoviruses, which normally infect rodents but are also infectious for human cells. Rommelaere and his team started by studying the cellular biology of their oncolytic effect. They went on to show, jointly with Dr. Karsten Geletneky of Heidelberg University Neurosurgery Hospital, that advanced glioblastomas in experimental animals regressed completely after treatment with parvoviruses and that these animals survived significantly longer than untreated fellow animals.

“Thus we had demonstrated that cancer treatment with parvoviruses can work. This is where we had to go on, because we saw a great chance of also using our viral therapy to help humans affected by glioblastoma, an extremely malignant type of brain tumor. But in order to further develop our project to clinical application we urgently needed a partner,” said Jean Rommelaere. The required preclinical studies involve too much effort – even for a large research institute like DKFZ.

It was in this phase that Oryx GmbH & Co KG joined the project. In January 2008, the Munich-based company signed a cooperation agreement with the German Cancer Research Center and Heidelberg University Hospital, which is also involved in the development of the viral therapy. Oryx specializes on taking research projects in cancer medicine through the preclinical and early clinical development stages and selling them to the pharmaceutical industry.

Working together with industrial partners, Oryx coordinated the large-scale technical production and subsequent pharmacology and toxicology testing of the therapeutic viruses as well as the approval procedure with the Paul Ehrlich Institute. Approval was finally given in the summer of this year – it is the first time that brain tumors may be treated with viruses in Europe.

“A cancer therapy with viruses is uncommon business for all parties involved, therefore the hurdles we jointly had to take to get the approval were high,” says Dr. Bernard Huber, Director of Oryx GmbH & Co KG. “We are all the more pleased that the clinical trial can finally start now.” Under the leadership of Dr. Karsten Geletneky and Prof. Andreas

Unterberg, the first patient has been treated earlier this week with parvoviruses prior to surgical removal of the tumor at Heidelberg University Neurosurgical Hospital.

Jean Rommelaere and Bernard Huber are convinced of the potential of the new therapy method: "We wish that our joint efforts will contribute to improving the dramatic situation of glioblastoma patients."