Tumor-attacking virus strikes with 'one-two punch'

December 1 2009

Ohio State University cancer researchers have developed a tumor-attacking virus that both kills brain-tumor cells and blocks the growth of new tumor blood vessels.

Their research shows that viruses designed to kill cancer cells - oncolytic viruses - might be more effective against aggressive brain tumors if they also carry a gene for a protein that inhibits blood-vessel growth.

The protein, called vasculostatin, is normally produced in the brain. In this study, an oncolytic virus containing the gene for this protein in some cases eliminated human glioblastoma tumors growing in animals and significantly slowed tumor recurrence in others. Glioblastomas, which characteristically have a high number of blood vessels, are the most common and devastating form of human brain cancer. People diagnosed with these tumors survive less than 15 months on average after diagnosis.

"This is the first study to report the effects of vasculostatin delivery into established tumors, and it supports further development of this novel virus as a possible cancer treatment," says study leader Balveen Kaur, associate professor of neurological surgery and a researcher with the Ohio State University Comprehensive Cancer Center-Arthur G. James Cancer Hospital and Richard J. Solove Research Institute. "Our findings suggest that this oncolytic virus is a safe and promising strategy to pursue for the treatment of human brain tumors.

"This study shows the potential of combining an oncolytic virus with a

natural blood-vessel growth inhibitor such as vasculostatin. Future studies will reveal the potential for safety and efficacy when used in combination with chemotherapy and radiation therapy," she says.

The findings were recently published online in the journal *Molecular Therapy*.

Jayson Hardcastle, a graduate student in Dr. Kaur's laboratory, injected the cancer-killing virus, called RAMBO (for Rapid Antiangiogenesis Mediated By Oncolytic virus), directly into human glioblastoma tumors growing either under the skin or in the brains of mice.

Of six animals with tumors under the skin, those treated with RAMBO survived an average of 54 days. In addition, three of the RAMBO mice were tumor-free at the end of the experiment. Control animals treated with a similar virus that lacked the vasculostatin gene, on the other hand, survived an average of 26 days and none were tumor-free.

Of the animals with a human glioblastoma in the brain, five were treated with RAMBO and lived an average of 54 days. One animal remained tumor-free for more than 120 days. Control animals, by comparison, lived an average of 26 days with no long-term survivors.

In another experiment, the investigators followed the course of tumor changes in animals with tumors in the brain. After an initial period of tumor shrinkage, the remaining cancer cells began regrowing around day 13 in animals given the virus that lacked the blood-vessel inhibitor. In animals treated with RAMBO, tumor regrowth didn't begin until about day 39.

"With additional research, this virus could lead to a new therapeutic strategy for combating cancer," Kaur says.

Source: Ohio State University Medical Center