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Oncolytic virus extends survival in medulloblastoma model

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A strain of measles virus engineered to kill cancer cells prolongs survival in a model of medulloblastoma that is disseminated in the fluid around the brain, according to a new study by researchers at Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute and the Mayo Clinic. Treatment with the oncolytic virus called MV-GFP extended survival of animals with disseminated human medulloblastoma up to 122 percent, with treated animals surviving 82 days on average versus 37 days for controls. Two of the eight treated animals were left cancer-free.

The findings, published online in the journal *Neuro-Oncology*, could lead to a safer, more effective therapy for medulloblastoma, and particularly for disseminated medulloblastoma, the researchers say.

Medulloblastoma accounts for 15 to 20 percent of all childhood brain tumors, with 350 to 400 new cases diagnosed annually in the United States.

Untreated, medulloblastoma is fatal. Current therapy for the disease involves surgery, multidrug chemotherapy and radiation therapy to the entire brain. Five-year survival is about 60 percent, but the extensive radiation therapy often leads to decreased intelligence.

Furthermore, in about 20 percent of newly diagnosed patients and 75 percent of patients with recurrent disease, the tumor has disseminated into the cerebrospinal fluid. Five-year survival for these children is less

than 20 percent.

"Patients whose tumor has spread into the fluid around the brain and spinal cord have an especially grim prognosis," says principal investigator Dr. Cory Raffel, professor and vice-chair of neurological surgery.

"Because dissemination of tumor carries a grave prognosis, any treatment that can effectively treat this condition while avoiding radiation therapy could potentially improve survival in these patients and quality of life for survivors."

For this study, Raffel and his collaborators used two human medulloblastoma cell lines that they labeled with firefly luciferase, making the cells bioluminescent and enabling the researchers to track them as they dispersed in the living animal and responded to treatment with the oncolytic virus.

Three or 14 days after the cancer cells were implanted in the brain; the oncolytic virus was injected at the same location in five doses.

In the first medulloblastoma cell line tested, treated animals lived an average of 82 days compared with 37 days for the controls. Two of the eight animals were cured of the disseminated disease, which was determined first according to bioluminescent imaging, then histologically.

In a second experiment using a more virulent human medulloblastoma cell line, treated animals survived 37 days versus 16 days for controls, with one animal left cancer free.

Currently, the investigators are conducting studies to determine optimal dosing of the virus in preparation for a phase I clinical trial in humans.