Modified measles virus shows potential for treating childhood brain tumors

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The use of modified measles virus may represent a new treatment for a childhood brain tumor known as medulloblastoma, according to a new study appearing in *Neuro-Oncology*.

Medulloblastoma is the most common malignant central nervous system tumor of childhood, accounting for about 20 percent of pediatric brain tumors. These tumors are located in the cerebellum, the area of the brain that controls balance and other complex motor functions. Refinements in treatment have increased the 5-year survival to close to 70 percent, but treatment still involves invasive surgery, radiation therapy and chemotherapy.

"There is still an urgent need to investigate alternative therapeutic approaches that are more effective and have less toxic side effects," said study lead author Corey Raffel, MD, PhD, chief of Neurosurgery at Nationwide Children's Hospital and a faculty member of The Ohio State University College of Medicine.

Vaccine strains of measles virus have been used to kill tumor cells in a number of tumor types including one type of adult brain tumor. One vaccine strain of measles, the Edmonston strain, targets the cell surface receptor CD46 to gain entry into susceptible cells. "This preference most likely explains the efficacy of Edmonston strains in killing tumor cells, given the high level of expression of CD46 in multiple tumor types," said Dr. Raffel. "It is also the reason we chose to explore a modified Edmonston's strain of measles virus for use in medulloblastoma."

The team's laboratory studies revealed that established medulloblastoma cell lines express the measles receptor, CD46 and that medulloblastoma specimens removed from patients have a high level of CD46 expression.

"Other oncolytic viruses have been explored as possible treatment modalities for medulloblastoma," said Dr. Raffel. "The fact that all of the surgical medulloblastoma specimens that we examined expressed the measles virus receptor leads us to believe that measles virus may have some advantages over other viruses."

Having demonstrated receptor expression, the team treated the medulloblastoma cell lines with the modified measles virus. Within 72 hours, all cell lines exhibited significant tumor cell death.

The team also administered the modified measles virus to mouse models of medulloblastoma, administering treatment every other day for 10 days. By the end of the study period, pathological review of the animals confirmed that two of the animals were free of tumor and the third had a very small amount of residual tumor. In eight of the eleven mice the primary tumor was eradicated.

"Our study demonstrates that a modified measles virus has therapeutic potential in the treatment of intracerebral medulloblastoma," said Dr. Raffel. "These results provide initial data to be pursued with additional studies toward the goal of using the virus in a clinical trial for the treatment of medulloblastoma. Measles virus therapy could be applied to the tumor bed following surgical resection to target microscopic residual disease. This approach could potentially alleviate the need for radiation and chemotherapy."

The data also suggest that the measles virus may be a potential therapy for tumors that have spread to the cerebral spinal fluid. "When tumor cells gain access to the cerebral spinal fluid and the subarachnoid space, current therapy is largely ineffective," said Dr. Raffel. We have preliminary data in the lab demonstrating efficacy of measles virus in treating disseminated tumor in a mouse model of CSF disease.

Researchers now plan to investigate the optimal

dose schedule for injection of the virus. They also intend to examine how modifications of the virus might lead to more effective treatment of the tumor. "Overall, the results suggest that use of modified measles virus may represent a new treatment for medulloblastoma," said Dr. Raffel.

Provided by Nationwide Children's Hospital