Cellular target may prove useful in treating deadly brain tumors

April 3 2009

Duke University researchers have identified a receptor on the surface of cells that may give them another avenue of attack against glioblastoma, the most common and most deadly type of brain cancer.

The neurokinin 1 receptor (NK1R), which may be expressed in all human glioblastoma cells, may prove to be an appropriate target for therapies aimed at treating these brain tumors, according to a study led by researchers in the Duke Department of Anesthesiology and the Preston Robert Tisch Brain Tumor Center at Duke.

"There are some previously identified cellular targets for therapy which are now being investigated in clinical trials, and the findings from our research represent potential alternate or complementary targets that may help patients facing this devastating disease," said Madan Kwatra, PhD, a researcher in Duke's department of anesthesiology, and senior investigator on this study. "Patients generally die from the disease within 18 months of glioblastoma diagnosis."

The results of the study were published in the March 30, 2009 online edition of the *Journal of Neurochemistry*. The study was funded by the National Institutes of Health.

The researchers examined stimulation of the receptor NK1R in human glioblastoma cells growing in a dish, and found that activation of NK1R led to the activation of Akt, a cellular protein that suppresses the natural cell death process.

"In human cancers, this would translate into a proliferation of cancer cell growth," said Kwatra.

The researchers also showed that blocking NK1R activity reduced Akt activity, which then led to greater cell death.

"This finding suggests that if we are able to block NK1R activity, we may have a better shot at stalling cancer growth," Kwatra said.

A previous study showed NK1R activity in 10 out of 10 glioblastomas and nine out of 12 astrocytomas, a lower-grade malignant brain tumor.

Current therapies to treat glioblastomas are directed toward blocking the activity of another cellular receptor called epithelial growth factor receptor (EGFR). A recent clinical trial using an EGFR inhibitor found that patients whose tumors expressed high levels of phosphorylated - or chemically altered - Akt did not respond to treatment, Kwatra said.

"This underscores the importance of discovering the origin of active Akt in glioblastomas," he said. "We propose that the elevated levels of phosphorylated Akt may come from active forms of NK1R, and it's possible that a better response might be obtained by simultaneously blocking EGFR and NK1R."

Future studies may examine the role of a NK1R inhibitor in glioblastoma patients, perhaps as a corollary to treatment with an EGFR blocker such as erlotinib, which is currently being studied in clinical trials.

"The FDA has already approved a drug for combating chemotherapy-induced nausea and vomiting that happens to be an NK1R inhibitor, so that might be a possibility for study in conjunction with erlotinib," Kwatra said.

Source: Duke University Medical Center