Loss of gene promotes brain-tumor development, reduces survival, study finds

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New research shows that loss of a gene called NFKBIA promotes the growth of glioblastoma multiforme, the most common and deadly form of brain cancer, and suggests that therapies that stabilize this gene may improve survival for certain glioblastoma patients.

The study was published recently in the New England Journal of Medicine.

"We show that NFKBIA status may be an independent predictor of survival in certain patients with glioblastoma," says senior coauthor Dr. Arnab Chakravarti, chair and professor of Radiation Oncology and co-director of the Brain Tumor Program at the Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James).

"We also show that this gene plays a key role in glioblastoma behavior, and that it could be useful for predicting treatment outcomes," he says.

An estimated 18, 500 new cases of glioblastoma occur annually among Americans, resulting in 12,760 deaths. Average survival after diagnosis is about 12 to 15 months.

Most cases of the disease are driven by over activity of a gene called EGFR (epidermal growth factor receptor). This study shows that loss of NFKBIA (nuclear factor of kappa-light polypeptide gene enhancer in B-cells inhibitor-alpha) and overexpression EGFR are equally potent at

driving glioblastoma development.

It also shows that glioblastoma tumors generally show either abnormally high levels of EGFR or loss of NFKBIA, but not both. Normal levels of both genes also occur.

Chakravarti, along with Markus Bredel, an adjunct associate professor of radiation oncology at Ohio State and their colleagues analyzed data from 790 cases of glioblastoma, which they divided into 10 study sets, for gene deletions, mutations, and expression of NFKBIA and EGFR.

Using glioblastoma cell lines and tumor cells from patients, they examined the influence of the NFKBIA gene on tumor-cell growth and sensitivity to temozolomide, the most effective chemotherapy for glioblastoma. Finally, they compared these findings with the outcomes of 570 glioblastoma patients.

These investigations showed the following:

- Restoring NFKBIA in tumor cells inhibited their growth and viability and increased the cells' sensitivity to temozolomide.
- Restoring NFKBIA suppresses the growth of glioblastoma cells that are driven by overexpression of EGFR.
- Patients with both copies of NFKBIA survive significantly longer than did patients with tumors that have lost a copy of the gene (131 weeks and 57 weeks, respectively).

Provided by Ohio State University Medical Center