



New Study Reveals Key Role for Immune System Cells in Brain Tumor Growth

December 15, 2008 — Current brain tumor therapies are designed to block the growth of the cancer cells within the tumor. Recent studies at Washington University have revealed a critical role for a specific type of immune system cells in brain tumor growth.

The study, which appears in the December 15th issue of the journal *Cancer Research*, demonstrates that specialized brain immune system cells, called microglia, provide important signals that promote brain tumor (glioma) growth in individuals with the inherited tumor predisposition syndrome, neurofibromatosis type 1 (NF1).

"By investigating the role of microglia in tumor growth control, we provide new opportunities for future glioma treatments" says principal investigator David H. Gutmann, M.D., Ph.D., the Donald O. Schnuck Family Professor of Neurology and Director of the Neurofibromatosis (NF) Clinic at St. Louis Children's Hospital. "Instead of relying solely on drugs that inhibit cancer cell growth, we are now in the unique position to develop therapies that target other cell types in the brain that promote glioma growth."

About one in 3,000 newborns has neurofibromatosis 1, in which every cell in the body has one normal and one mutated copy of a gene called *Nf1*. If a cell's normal copy also is mutated, tumors can form. Children with neurofibromatosis 1 are therefore predisposed to developing a variety of serious complications as they grow older, including skin, spine and brain cancers.

Previous studies by Gutmann and colleagues demonstrated that microglia from mice genetically-engineered to resemble patients with NF1 have unique biological properties that lead to increased glioma growth. In the current study, they identified the signaling pathway in microglia responsible for increasing tumor growth and show that blocking the activity of this pathway restores these *Nf1* mutant microglia to normal. They also showed that inhibiting microglia function in live mice with optic glioma reduced the growth of these brain tumors.

These studies coupled with others currently ongoing at the Washington University NF Center provide strong experimental evidence that brain tumors in children respond to instructive cues from the local brain environment. "Our results suggest that future therapies for brain tumors may involve a combination of treatments that target the abnormal cell types found in the tumor environment and therapies that inhibit cancer cell growth," Gutmann says.

Daginakatte GC, Gianino SM, Zhao NW, Parsadarian AS, and Gutmann DH. Increased c-Jun-NH2-kinase signaling in neurofibromatosis-1 heterozygous microglia drives microglia activation and promotes optic glioma proliferation. *Cancer Research*, December 15, 2008.

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