

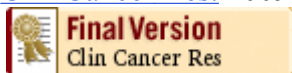


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1: [Clin Cancer Res.](#) 2009 May 15;15(10):3519-29.



**Folate supplementation limits the aggressiveness of glioma via the remethylation of DNA repeats element and genes governing apoptosis and proliferation.**

[Hervouet E](#), [Debien E](#), [Campion L](#), [Charbord J](#), [Menanteau J](#), [Vallette FM](#), [Cartron PF](#).

Institut National de la Sante et de la Recherche Medicale U892, Centre de Recherche en Cancérologie, Equipe Apoptose et Progression Tumorale, Nantes, France.

**PURPOSE:** We have investigated whether the folate supplementation could be used to limit the aggressiveness of glioma through the DNA remethylation because (a) the cancer genome is characterized by a low level of DNA methylation (or 5-methylcytosine, 5 mC); and (b) folate is the main generator of S-adenosyl-methionine, the methyl donor molecule in the DNA methylation reaction catalyzed by the DNA methyltransferases. **EXPERIMENTAL DESIGN:** The effects of folate supplementations were analyzed on the global DNA methylation status, the methylation status of DNA repeat element, the sensitivity of temozolomide-induced apoptosis, and the proliferation index of glioma cells. Finally, we analyzed whether the DNA methylation level could be used as a prognostic factor and/or a biomarker in an antiglioma therapy using folate supplementation as an adjuvant. **RESULTS:** Our data show that gliomagenesis is accompanied by a reduction in 5 mC levels and that this low level of 5 mC is a poor prognostic factor in Glioblastoma Multiforme patients. We also show that folate supplementation enhanced the DNA remethylation through the Sp1/Sp3-mediated transcriptional up-regulation of genes coding for Dnmt3a and Dnmt3b proteins, two de novo methyltransferases. Finally, we show that the folate-induced DNA methylation limits proliferation and increases the sensitivity to temozolomide-induced apoptosis in glioma cells through methylation of the genes implicated in these processes (PDGF-B, MGMT, survivin, and bcl-w). **CONCLUSION:** This study suggests that folate supplementation could be a promising adjuvant for the future design of antiglioma therapies in preclinical and/or clinical studies.

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