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High incidence of *MGMT* promoter methylation in primary glioblastomas without correlation with *TP53* gene mutations

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Abstract

O⁶-methylguanine DNA methyltransferase (*MGMT*) reduces cytotoxicity of therapeutic or environmental alkylating agents. *MGMT* promoter methylation has been associated with *TP53* G: C to A: T transition mutations in various types of cancers, and with poor prognosis in patients who did not receive chemotherapy. Mutations of *TP53* are more frequent in secondary than in primary glioblastoma, thus the expected *MGMT* promoter methylation was low in primary glioblastoma. Glioblastoma patients with *MGMT* promoter methylation showed better response to chemotherapy based on alkylating agents and longer survival than patients without *MGMT* methylation. We examined 32 primary glioblastomas, treated with radiotherapy and surgery, for *TP53* mutation by direct sequencing and *MGMT* promoter methylation by methylation-specific PCR. *MGMT* promoter methylation and *TP53* mutations were detected in 72% and 31% of primary glioblastoma, respectively. Although not statistically significant, the frequency of *TP53* G: C to A: T mutations were higher in cases with (26%) than without (11%) *MGMT* promoter methylation ($p=0.376$). *MGMT* promoter methylation had no impact on patient survival. Our data indicate that *MGMT* promoter methylation occurs frequently in primary glioblastoma, but does not lead to G: C to A: T *TP53* mutations, has no independent prognostic value and is not a predictive marker unless glioblastoma patients are treated with chemotherapy.

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