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Primer extension based quantitative polymerase chain reaction reveals consistent differences in the methylation status of the MGMT promoter in diffusely infiltrating gliomas (WHO grade II-IV) of adults.

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Abstract

Diffusely infiltrating gliomas (WHO grade II-IV) are the most common primary brain tumours in adults. These tumours are not amenable to cure by surgery alone, so suitable biomarkers for adjuvant modalities are required to guide therapeutic decision-making. Epigenetic silencing of the O(6)-methylguanine-DNA methyltransferase (MGMT) gene by promoter methylation has been associated with longer survival of patients with high-grade gliomas who receive alkylating chemotherapy; and molecular testing for the methylation status of the MGMT promoter sequence is regarded as among the most relevant of such markers. We have developed a primer extension-based assay adapted to formalin-fixed paraffin-embedded tissues that enables quantitative assessment of the methylation status of the MGMT promoter. The assay is very sensitive, highly reproducible, and provides valid test results in nearly 100% of cases. Our results indicate that oligodendrogliomas, empirically known to have a relatively favourable prognosis, are also the most homogeneous entities in terms of MGMT promoter methylation. Conversely, astrocytomas, which are more prone to spontaneous progression to higher grade malignancy, are significantly more heterogeneous. In addition, we show that the degree of promoter methylation correlates with the prevalence of loss of heterozygosity on chromosome arm 1p in the oligodendroglioma group, but not the astrocytoma group. Our results may have potentially important implications for clinical molecular diagnosis.

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