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MGMT promoter methylation in malignant gliomas.

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Abstract

The O(6)-methylguanine-DNA methyltransferase (MGMT) gene is located at chromosome 10q26 and codes for a DNA repair enzyme that-if active-can counteract the effects of alkylating chemotherapy. Malignant gliomas often have the MGMT gene inactivated due to aberrant methylation of its promoter region. The assessment of the MGMT promoter methylation status has become of clinical relevance as a molecular marker associated with response to alkylating chemotherapy and prolonged survival of glioblastoma patients. MGMT promoter methylation testing is also on the merge of being used as a marker for patient selection within clinical trials, e.g., the current CENTRIC trial that is specifically focusing on patients with MGMT promoter-methylated glioblastomas. In anaplastic gliomas, MGMT promoter methylation is a favorable prognostic marker independent of the type of therapy, i.e., radio- or chemotherapy. This occurrence might be associated with the high incidence of other prognostically favorable molecular markers in these tumors, such as IDH1 mutation, 1p/19q deletion or yet to be identified novel aberrations. A variety of different methods are being used to assess MGMT promoter methylation in clinical samples, which may give rise to inter-laboratory variations in test results. Immunohistochemical determination of MGMT protein expression has not proven reliable for diagnostic purposes. This brief review article aims to summarize the main aspects of MGMT promoter methylation testing in contemporary neuro-oncology, in particular its value as a clinically useful molecular marker, putting it into the context of other molecular markers of clinical use in gliomas of adult patients.

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