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MGMT promoter hypermethylation is a frequent, early, and consistent event in astrocytoma progression, and not correlated with TP53 mutation.

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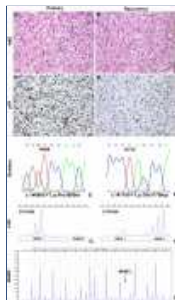
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Abstract

Hypermethylation of the MGMT gene promoter and mutation of the TP53 tumor-suppressor gene are frequently present in diffuse astrocytomas. However, there is only anecdotal information about MGMT methylation status and TP53 mutations during progression of low-grade diffuse astrocytoma (AII) to anaplastic astrocytoma (AIII) and secondary glioblastoma (sGB). In this study biopsy specimens from 51 patients with astrocytic tumors with radiologically proved progression from low to high-grade malignancy were investigated for the presence and consistency of MGMT promoter hypermethylation and TP53 mutations. For 27 patients biopsy samples both of primary tumors and their recurrences were available. For the other 24 patients histology of either the low-grade lesion or the high-grade recurrence was available. It was found that MGMT promoter hypermethylation and TP53 mutations are both frequent and early events in the progression of astrocytomas and that their status is consistent over time. No correlation was found between MGMT methylation status and the presence of TP53 mutations. In addition, no correlation was found between MGMT promoter hypermethylation and the type of TP53 mutations. These results argue against the putative TP53 G:C>A:T transition mutations suggested to occur preferentially in MGMT hypermethylated tumors.

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