Abstract
The scaffold protein A-kinase anchor protein 12 (AKAP12) exerts tumor suppressor activity and is downregulated in several tumor entities. We characterized AKAP12 expression and regulation in astrocytomas, including pilocytic and diffusely infiltrating astrocytomas. We examined 194 human gliomas and 23 normal brain white matter samples by immunohistochemistry or immunoblotting for AKAP12 expression. We further performed quantitative methylation analysis of the AKAP12 promoter by MassARRAY® of normal brain, World Health Organization (WHO) grade I to IV astrocytomas, and glioma cell lines. Our results show that AKAP12 is expressed in a perivascular distribution in normal CNS, strongly upregulated in tumor cells in pilocytic astrocytomas, and weakly expressed in diffuse astrocytomas of WHO grade II to IV. Methylation analyses revealed specific hypermethylation of AKAP12α promoter in WHO grade II to IV astrocytomas. Restoration experiments using 5-aza-2'-deoxycytidine in primary glioblastoma cells decreased AKAP12α promoter methylation and markedly increased AKAP12α mRNA levels. In summary, we demonstrate that AKAP12 is differentially expressed in human astrocytomas showing high expression in pilocytic but low expression in diffuse astrocytomas of all WHO-grades. Our results further indicate that epigenetic mechanisms are involved in silencing AKAP12 in diffuse astrocytomas; however, a tumor suppressive role of AKAP12 in distinct astrocytoma subtypes remains to be determined.

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