Epigenetic aberrations and therapeutic implications in gliomas.

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Abstract
Almost all cancer cells have multiple epigenetic abnormalities, which combine with genetic changes to affect many cellular processes, including cell proliferation and invasion, by silencing tumor-suppressor genes. In this review, we focus on the epigenetic mechanisms of DNA hypomethylation and CpG island hypermethylation in gliomas. Aberrant hypermethylation in promoter CpG islands has been recognized as a key mechanism involved in the silencing of cancer-associated genes and occurs at genes with diverse functions related to tumorigenesis and tumor progression. Such promoter hypermethylation can modulate the sensitivity of glioblastomas to drugs and radiotherapy. As an example, the methylation of the O6-methylguanine DNA methyltransferase (MGMT) promoter is a specific predictive biomarker of tumor responsiveness to chemotherapy with alkylating agents. Further, we reviewed reports on pyrosequencing - a simple technique for the accurate and quantitative analysis of DNA methylation. We believe that the quantification of MGMT methylation by pyrosequencing might enable the selection of patients who are most likely to benefit from chemotherapy. Finally, we also evaluated the potential of de novo NY-ESO-1, the most immunogenic cancer/testis antigen (CTA) discovered thus far, as an immunotherapy target. The use of potent epigenetics-based therapy for cancer cells might restore the abnormally regulated epigenomes to a more normal state through epigenetic reprogramming. Thus, epigenetic therapy may be a promising and potent treatment for human neoplasia.

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