

Display Settings: Abstract



Oncol Rep. 2011 Jul 18. doi: 10.3892/or.2011.1393. [Epub ahead of print]

## Expression of glioma stem cell marker CD133 and O6-methylguanine-DNA methyltransferase is associated with resistance to radiotherapy in gliomas.

He J, Shan Z, Li L, Liu F, Liu Z, Song M, Zhu H.

Department of Pathology, Wuxi Tumor Research Institute, the Fourth Affiliated Hospital of Soochow University, 200 Huihe Road, Wuxi 214062, Jiangsu, P.R. China.

### Abstract

In the present study, we investigated the prognostic roles of the O6-methylguanine-DNA methyltransferase (MGMT) gene methylation status, the protein profiles of MGMT, and the glioma stem cell (GSC) marker CD133 in malignant glioma resistance to radiotherapy. The proliferation of glioma cells was assessed using a clonogenic survival assay and flow cytometry. CD133 expression was assessed in SHG-44-GSCs using RT-PCR and flow cytometry. MGMT exhibited resistance to radiation in the SHG-44-GSCs using siRNA transfection. The effects of the siRNA on mRNA and protein expression of MGMT in SHG-44-GSCs were detected using semi-quantitative reverse transcription polymerase chain reaction (qRT-PCR) and Western blotting. MGMT methylation status, MGMT and CD133 expression profiles were assessed in 59 malignant glioma patients using methylation-specific polymerase chain reaction (MSP), and immunohistochemistry. In vitro, SHG-44-GSCs exhibited a characteristic resistance to radiation that was not observed in SHG-44 cells. This resistance was attributed to the unmethylated status of the MGMT promoter and to high expression levels of MGMT mRNA in the glioma cells. In these patients, the CD133 marker, but not MGMT promoter methylation or MGMT protein level, was associated with resistance to radiotherapy (n=59; hazard ratio=2.838; 95% CI, 1.725-7.597; p=0.001). The median progression-free survival (PFS) among patients with the CD133 marker was 14 months, whereas it was 35 months in patients without CD133 (p=0.001). Notably, co-expression of the methylated MGMT promoter and the CD133 marker was associated with the poorest outcome in patients with gliomas treated by radiotherapy; in these patients, PFS was 7 months. These results suggest that assessment of GSC MGMT and CD133 levels will guide future clinical targeted therapies and stratify glioma patient treatment regimens. High expression levels of the CD133 protein could be used as a predictor for poor survival in patients treated with radiotherapy.

PMID: 21769436 [PubMed - as supplied by publisher]

**LinkOut - more resources**