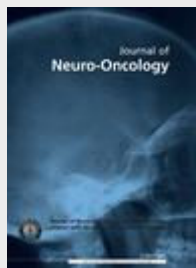




## Journal Article



## Hypermethylation of the proapoptotic gene *TMS1/ASC*: prognostic importance in glioblastoma multiforme

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Ramon Martinez<sup>1, 3</sup> , Gabriele Schackert<sup>1</sup> and Manel Esteller<sup>2</sup>

- (1) Department of Neurosurgery, University of Dresden, Fetscherstr. 74, D-01307 Dresden, Germany
- (2) Cancer Epigenetics Laboratory, Spanish National Cancer Centre (CNIO), Melchor Fernandez Almagro 3, E-28029 Madrid, Spain
- (3) Department of Neurosurgery, Klinikum Fulda, Academic Hospital Philipps University Marburg, Pacelliallee 4, D-36043 Fulda, Germany

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**Abstract** The identification of clinical subsets of glioblastomas (GBM) associated with different molecular genetic profiles had opened the possibility to design tailored therapies to individual patients. One of the most intrigued subtypes is the long-term survival (LTS) GBM, which responds better to current therapies. The present investigation on GBM from 50 consecutive GBM displaying classic survival and seven LTS GBM is based on molecular epigenetic, clinical and histopathological analyses. Our aim was to recognize biomarkers useful to distinguish LTS from classic GBM. We analyzed the promoter methylation status of key regulator genes implicated in tumor invasion (*TIMP2*, *TIMP3*), apoptosis and inflammation (*TMS1/ASC*, *DAPK*) as well as overall survival, therapy status and tumor pathological features. For the first purpose a methylation-specific PCR approach was performed to analyze the CpG island promoter methylation status of each gene. The overall *TMS1/ASC* methylation rate in the 57 analyzed tumors was 21.05%. Hypermethylation of *TMS1/ASC* was significantly more frequent in LTS GBM (57.1% vs. 16%,  $P = 0.029$ , Fisher's exact test). *DAPK* promoter hypermethylation was only observed in the LTS subset (14.3%) whereas *TIMP2* and *TIMP3* were unmethylated in both GBM collectives. Our results strongly suggest that, compared to classic GBM, LTS GBM display distinct epigenetic characteristics which might provide additional prognostic biomarkers for the assessment of this malignancy.

**Keywords** Glioblastoma - Long-term survival - Epigenetic - Hypermethylation - *TMS1* - *DAPK* - *TIMP*



**Ramon Martinez**

**Email:** ramon.martinez@gmx.net

**Phone:** +49-661-845801

**Fax:** +49-661-845802

References secured to subscribers.

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