Abstract:

OBJECT: The mismatch repair (MMR) system has previously been implicated in acquired chemoresistance in malignant gliomas in humans. Its impact on the primary chemoresistance in glioblastoma multiforme (GBM) has not been determined in detail, however.

METHODS: The authors investigated the expression of both the MMR genes (hMSH2, hMLH1, hPMS1, hPMS2, and hMSH6) at the transcriptional level through reverse transcription-polymerase chain reaction and the hMSH2 protein through Western blot and immunohistochemical analysis of tumor tissue and primary cell cultures of 25 in vitro human de novo GBMs without prior experimental treatment. Results of these analyses were compared with data on in vitro chemoresistance to nine drugs that are in general use in glioma therapy.

All MMR genes were expressed in the GBMs, with no significant difference among the individual tumors except in one respect; that is, GBMs showed either relatively high levels or barely detectable levels of hMSH2 messenger (m)RNA and protein expression. All multiresistant tumors demonstrated high hMSH2 expression, and all but two of the sensitive tumors exhibited low hMSH2 mRNA levels.

CONCLUSIONS: Analysis of the data indicates that functional alterations of the MMR system are involved in the primary drug resistance in in vitro human malignant gliomas. Analysis of hMSH2
expression might therefore predict therapeutic responses in humans with GBMs.