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Radiotherapy resistance acquisition in Glioblastoma. Role of SOCS1 and SOCS3

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Background. Glioblastoma multiforme (GBM) is a poor prognosis type of tumour due to its resistance to chemo and radiotherapy. *SOCS1* and *SOCS3* have been associated with tumour progression and response to treatments in different kinds of cancers, including GBM. In this study, cell lines of *IDH*-wildtype GBM from primary cultures were obtained, and the role of *SOCS1* and *SOCS3* in the radiotherapy response was analyzed.

Methods. Tissue culture, Gene expression analysis, DNA sequencing, Flow cytometry analysis of cell cycle, RNAi Transfection, Immunohistochemistry and Confocal microscopy.

RESULTS. Fifty-two brain aspirates from GBM patients were processed, and six new cell lines of *IDH* -wildtype GBM were established. These new cell lines were characterized according to the WHO classification of CNS tumours. *SOCS1* and *SOCS3* expression levels were determined, at mRNA level by Q-PCR, and protein level by immunocytochemistry. The results showed that *SOCS1* at and *SOCS3* are overexpressed in GBM, as compared to a non-tumoral brain RNA pool. *SOCS1* and *SOCS3* expression were reduced by siRNA, and it was found that *SOCS3* inhibition increases radiorresistance in GBM cell lines, suggesting a key role of *SOCS3* in radiorresistant acquisition. Furthermore, overexpression of *SOCS3*, under a heterologous promoter, in a radiotherapy resistant GBM cell line increased its radiosensitivity, supporting an important implication of *SOCS3* in radiotherapy resistance acquisition. Thus, *SOCS3* signal transduction pathway (JAK/STAT) could be useful to unmask new putative targets to improve radiotherapy response in GBM.

Conclusion . Our results demonstrate an important implication of *SOCS3* in radiotherapy resistance acquisition in GBM.

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