Stemness Markers Detection In The Periphery Of Glioblastomas And Glioblastoma Ability To Generate Glioma Stem Cells: Clinical Correlations.

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Abstract

BACKGROUND: Recent studies suggested glioma stem cells (GSCs) are key contributors to GBM therapeutic resistance and are responsible for GBM recurrence.

METHODS: Our aim was to characterize the phenotype of cancer cells in the core and periphery of 20 GBMs, correlating clinical outcome to the ability to form GSCs and distinguishing survival based on Ki67 staining.

RESULTS: Results showed similar levels of MGMT in the core and in the periphery of GBMs; whereas the Ki67 was reduced in the periphery. Similar levels of stemness markers in the periphery and in the core of all GBMs cultures were found. Only those cells expressing > 30% SOX2 levels were able to produce neurospheres. The immunophenotypic analysis showed higher levels of stemness markers in GSCs cultures than in all GBM primary cultures. Finally we noted that GSCs in vitro production and coexpression of Ki67>5% negatively correlated with outcome.

CONCLUSIONS: Not all GBM cultures can generate GSCs and this capacity is linked to >30% SOX2 levels. The ability to form spheres negatively correlated to survival and the detection of >5% Ki67 levels may be useful to identify subjects at risk of disease progression. Therefore the presence of GSCs-/SOX-2-/Ki67- cells might be regarded as a new prognostic factor. The presence of stemness markers and MGMT in the periphery of GBMs may be the reason for
treatment failure and recurrence. The development of stem cell-targeted therapies and the elaboration of more aggressive treatments represent an opportunity to eliminate the GBM source and the nidus of recurrence.

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**KEYWORDS:** Glioblastoma; cancer stem cells; overall survival; progression free survival; stemness markers

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