Glioblastoma Multiforme: Putative Stem Cell Hierachy



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Introduction

Glioblastoma Multiforme (GBM) the most aggressive form of brain glioma, is associated with a median survival of 25 months. Cancer stem cells (CSCs) have been reported to express stem cell markers and have been proposed to be the origin of many cancers, including GBM. This study was aimed at characterizing the CSC population within GBM tissue for the CSC markers SALL4, OCT4, SOX2, pSTAT3 and NANOG. Furthermore we have researched some of the properties of the neurospheres derived from freshly

acquired surgical GBM samples and investigated them for the expression of stem cell markers.

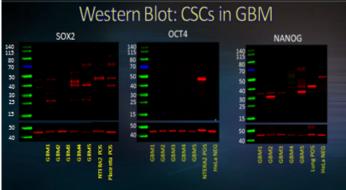
Methods

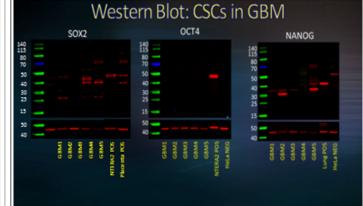
Immunohistochemistry was performed on seven GBM samples for the stem cell markers SALL4, OCT4, SOX2, NANOG and pSTAT3. Nanostring mRNA analysis was performed on five of the IHC cohort for the transcriptional analyses of the same stem cell markers. Cells from three surgically excised samples from the IHC cohort were grown in culture and stained for Stem cell markers, which has been associated with cancer stem cells.

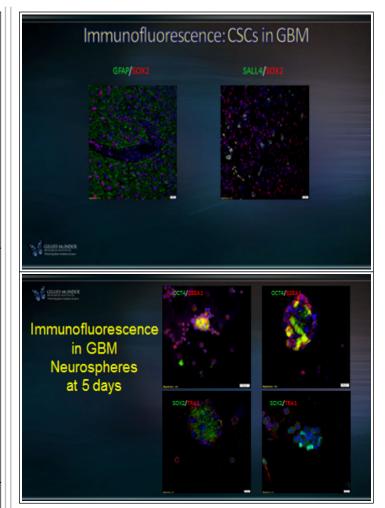
Results

IHC demonstrated a significant number of cells from GBM strongly expressed SOX2 and pSTAT3. A subset of these also weakly expressed OCT4, SALL4 and NANOG. Nanostring analysis demonstrated the expression of mRNA transcripts for these same markers. Western analysis showed similar patterns of expression, but OCT4 and SALL4 were not detected in these samples (for all results see Bradshaw et al, Front Surg, 2016). Cultures of GBM tissue revealed the growth of neurospheres at different timelines. The 5 day old spheres showed strong expression of SOX2 but also OCT4.









Conclusions

The expression of the stem cell markers within GBM highlights the identification of putative presence of CSCs in this tumor. The greater abundance of SOX2 and pSTAT3 with less for SALL4, OCT4 and NANOG, suggests a hierarchy of CSCs within GBM with the latter population potentially being the most primitive CSC in GBM, and a potential target for the development of future safer treatment options.