

TITLE

Inhibition of Glioma Stem Cells by targeting OncomiR 138.

ABSTRACT

Malignant gliomas are the most aggressive forms of brain tumors, associated with high rates of morbidity and mortality. Recurrence and tumorigenesis are attributed to a subpopulation of tumor-initiating glioma stem cells (GSCs) that are intrinsically resistant to therapy. Initiation and progression of gliomas have been linked to alterations in microRNA expression. Here, we report the identification of microRNA-138 (miR-138) as a molecular signature of GSCs and demonstrate a vital role for miR-138 in promoting growth and survival of bona fide tumor-initiating cells with self-renewal potential. Sequence-specific functional inhibition of miR-138 prevents tumorsphere formation in vitro and impedes tumorigenesis in vivo. We delineate the components of the miR-138 regulatory network by loss-of-function analysis to identify specific regulators of apoptosis. Finally, the higher expression of miR-138 in GSCs compared to non-neoplastic tissue and association with tumor recurrence and survival highlights the clinical significance of miR-138 as a prognostic biomarker and a therapeutic target for treatment of malignant gliomas.