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### microRNA-34a is tumor suppressive in brain tumors and glioma stem cells.

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#### Abstract

We recently found that microRNA-34a (miR-34a) is downregulated in human glioma tumors as compared to normal brain, and that miR-34a levels in mutant-p53 gliomas were lower than in wildtype-p53 tumors. We showed that miR-34a expression in glioma and medulloblastoma cells inhibits cell proliferation, G(1)/S cell cycle progression, cell survival, cell migration and cell invasion, but that miR-34a expression in human astrocytes does not affect cell survival and cell cycle. We uncovered the oncogenes c-Met, Notch-1 and Notch-2 as direct targets of miR-34a that are inhibited by miR-34a transfection. We found that c-Met levels in human glioma specimens inversely correlate with miR-34a levels. We showed that c-Met and Notch partially mediate the inhibitory effects of miR-34a on cell proliferation and cell death. We also found that miR-34a expression inhibits in vivo glioma xenograft growth. We concluded that miR-34a is a potential tumor suppressor in brain tumors that acts by targeting multiple oncogenes. In this extra view, we briefly review and discuss the implications of these findings and present new data on the effects of miR-34a in glioma stem cells. The new data show that miR-34a expression inhibits various malignancy endpoints in glioma stem cells. Importantly, they also show for the first time that miR-34a expression induces glioma stem cell differentiation. Altogether, the data suggest that miR-34a is a tumor suppressor and a potential potent therapeutic agent that acts by targeting multiple oncogenic pathways in brain tumors and by inducing the differentiation of cancer stem cells.

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