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Human glioma growth is controlled by microRNA-10b.

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Abstract

MicroRNA (miRNA) expression profiling studies revealed a number of miRNAs dysregulated in the malignant brain tumor, glioblastoma. Molecular functions of these miRNAs in gliomagenesis are mainly unknown. We show that inhibition of miR-10b, a miRNA not expressed in human brain and strongly up-regulated in both low-grade and high-grade gliomas, reduces glioma cell growth by cell cycle arrest and apoptosis. These cellular responses are mediated by augmented expression of the direct targets of miR-10b, including BCL2L1/Bim, TFAP2C/AP-2gamma, CDKN2A/p16, and CDKN1A/p21, which normally protect cells from uncontrolled growth. Analysis of The Cancer Genome Atlas (TCGA) expression dataset reveals a strong positive correlation between numerous genes sustaining cellular growth and miR-10b levels in human glioblastomas, while pro-apoptotic genes anti-correlate with the expression of miR-10b. Furthermore, survival of glioblastoma patients expressing high levels of miR-10 family members is significantly reduced in comparison to patients with low miR-10 levels, indicating that miR-10 may contribute to glioma growth in vivo. Finally, inhibition of miR-10b in a mouse model of human glioma results in significant reduction of tumor growth. Altogether, our experiments validate an important role of miR-10b in gliomagenesis and suggest the possibility of its future use as a therapeutic target in gliomas.

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