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MIR-451 and Imatinib mesylate inhibit tumor growth of Glioblastoma stem cells

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Abstract

We examined the microRNA profiles of Glioblastoma stem (CD133+) and non-stem (CD133-) cell populations and found up-regulation of several miRs in the CD133- cells, including *miR-451*, *miR-486*, and *miR-425*, some of which may be involved in regulation of brain differentiation. Transfection of GBM cells with the above miRs inhibited neurosphere formation and transfection with the mature miR-451 dispersed neurospheres, and inhibited GBM cell growth. Furthermore, transfection of *miR-451* combined with Imatinib mesylate treatment had a cooperative effect in dispersal of GBM neurospheres. In addition, we identified a target site for SMAD in the promoter region of miR-451 and showed that SMAD3 and 4 activate such a promoter-luciferase construct. Transfection of SMAD in GBM cells inhibited their growth, suggesting that SMAD may drive GBM stem cells to differentiate to CD133- cells through up-regulation of miR-451 and reduces their tumorigenicity. Identification of additional miRs and target genes that regulate GBM stem cells may provide new potential drugs for therapy.

Keywords: Stem cells; Neurospheres; MicroRNA; Combination therapy

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