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Methylation-mediated miR-155-FAM133A axis contributes to the attenuated invasion and migration of *IDH* mutant gliomas

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Abstract:

Gliomas with *isocitrate dehydrogenases* genes mutation (IDH^{MT}) were found to be less aggressive than their wildtype (IDH^{WT}) counterparts. However, the mechanism remains unclear. The current study aims to investigate the role of silenced oncogenic microRNAs in IDH^{MT} gliomas, which were largely ignored and may contribute to the less aggressive behavior of IDH^{MT} gliomas. Microarrays, bioinformatics analysis of the data from TCGA and qPCR analysis of samples from our experimental cohort (LGG: IDH^{WT}=10, IDH^{MT}=31; GBM: IDH^{WT}=34, IDH^{MT}=9) were performed. The results show that miR-155 was consistently down-regulated in IDH^{MT} gliomas. Establishment of $IDH1^{R132H}$ overexpressing glioma cell line and bisulfite sequencing PCR suggested that miR-155 down-regulation was associated with $IDH1^{R132H}$ mutation induced promoter CpG islands methylation. The cancer testis antigen FAM133A is a direct downstream target of miR-155 and is a negative regulator of glioma invasion and migration possibly by regulating matrix metallopeptidase 14 (MMP14). Together, we found that methylation-regulated miR-155-FAM133A axis may contribute to the attenuated invasion and migration of IDH^{MT} gliomas by targeting MMP14.

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