MIR 155

Targeting MIR155HG in glioma: a novel approach [1].

Chen et al. analysed the database for expression profiles and clinical specimens of various grades of glioma to assess microRNA-155-3p (miR 155-3p) expression. The role of miR-155-3p in glioblastoma, cell cycle, cell proliferation, apoptosis and resistance to temozolomide was assessed in vitro through flow cytometry and cell proliferation assays. Bioinformatics analyses, and assays using luciferase reporter, and immunoblotting revealed that miR-155-3p targets Six1 and that the relationship between glioma and healthy brain tissues was significantly inverse. In rescue experiments, overexpressed Six1 revoked the changes in cell cycle distribution, proliferation and resistance to temozolomide estimated by apoptosis induced by overexpressed miR-155-3p. MiR-155-3p inhibition reduced glioma cell growth and proliferation in the brain of a mouse model and increased the survival of mice with gliomas. Thus, miR-155-3p modulates Six1 expression and facilitates the progression of glioblastoma and resistance to temozolomide and may act as a novel diagnostic biomarker and a target for glioma treatment [2].

Huang et al., found that methylation-regulated miR-155-FAM133A axis may contribute to the attenuated invasion and migration of IDHMT gliomas by targeting MMP14 [3].

MIR 155 host gene (MIR155HG) is a Long non-coding RNA that has been considered as the primary micro (mi)RNA of miR-155. MIR155HG plays an essential role in hematopoiesis, inflammation, and tumorigenesis.

A study investigated the clinical significance, biological function, mechanisms, and small-molecule inhibitors of the MIR155HG/miR-155 axis in glioma.

Wu et al. analyzed the expression of the MIR155HG/miR-155 axis and the correlation with glioma grade and patient survival using 2 different glioma gene expression datasets. Biological significance was elucidated through a series of in vitro and in vivo experiments. Furthermore, we conducted a high-throughput screening for small molecules to identify a potential inhibitor of the MIR155HG/miR-155 axis.

Increased MIR155HG was associated with glioma grade, mesenchymal transition, and poor prognosis. Functionally, MIR155HG reduction by small interfering RNA inhibited cell proliferation, migration, invasion, and orthotopic glioma growth by repressing the generation of its derivatives miR-155-5p and miR-155-3p. Bioinformatics and luciferase reporter assays revealed that protocadherin 9 and protocadherin 7, which act as tumor suppressors by inhibiting the Wnt/β-catenin pathway, were direct targets of miR-155-5p and miR-155-3p, respectively. Finally, we identified NSC141562 as a potent small-molecule inhibitor of the MIR155HG/miR-155 axis.

The results demonstrate that the MIR155HG/miR-155 axis plays a critical role in facilitating glioma progression and serves as a prognostic factor for patient survival in glioblastoma. High-throughput screening indicated that the MIR155HG/miR-155 axis inhibitor NSC141562 may be a useful candidate anti-glioma drug [4].

Schliesser et al., performed unbiased DNA methylation screens that revealed 12 putative MicroRNA promoter regions with differential DNA methylation in anaplastic gliomas. Methylation of these candidate regions was validated in different independent patient cohorts revealing a set of MicroRNA promoter regions with prognostic relevance across data sets. Of those, miR-155 promoter methylation and miR-155 expression were negatively correlated and especially the methylation showed superior correlation with patient survival compared to established biomarkers.Functional examinations in malignant glioma cells further cemented the relevance of miR-155 for tumor cell viability with transient and stable modifications indicating an onco-MicroRNA activity. MiR-155 also conferred resistance towards alkylating temozolomide and radiotherapy as consequence of nuclear factor kappa (NFκB) activation.Preconditioning glioma cells with an NFκB inhibitor reduced therapy resistance of miR-155 overexpressing cells. These cells resembled tumors with a low methylation of the miR-155 promoter and thus mir-155 or NFκB inhibition may provide treatment options with a special focus on patients with IDH wildtype tumors [5].

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