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Hsa_circ_034367 regulates the progression of SHH-type medulloblastoma through the has-miR-17-3p/DICER1 axis

Abstract:

Background: Medulloblastoma is the most common malignant brain tumor in children, but its pathogenesis is unknown and there is a lack of early diagnostic markers or effective therapeutic targets. circRNA is a class of endogenous non-coding RNAs that regulate gene expression in eukaryotes. Hsa_circ_034367 is a newly discovered circRNA highly expressed in SHH-type medulloblastoma. The role and mechanism of CircRNA in SHH-type medulloblastoma remain to be further elucidated.

Methods: After ethical approval, several samples of medulloblastoma were obtained in our hospital, and adjacent tissues were obtained at the same time. By whole transcriptome sequencing and bioinformatics analysis, circRNA with high expression was screened. The expression pattern of hsa_circ_034367 in medulloblastoma was detected by Sanger sequencing and Northern blots. Real-time fluorescence quantitative PCR was used to detect the expression of hsa_circ_034367, has-miR-17-3p and DICER1. Lentivirus-infected medulloblastoma cell lines daoy and uw228 were constructed, and cell proliferation, migration, invasion and apoptosis were detected by MTT assay, colony formation assay, transwell assay, Celltier-GLO fluorescence cell viability assay and flow cytometry. In addition, the interaction between hsa_circ_034367, has-miR-17-3p and DICER1 was examined by dual luciferase reporting assay and RNA drop-down assay. DICER1 protein expression was detected by Western blot. To investigate the role of hsa_circ_034367 in the growth of medulloblastoma tumors in vivo by Patient-derived tumor xenograft (PDX) model.

Results: Hsa_circ_034367 was overexpressed in medulloblastoma tissues and cells, and its silence could inhibit the proliferation, migration and invasion of medulloblastoma and accelerate cell apoptosis. Has-miR-17-3p can be wiped by hsa_circ_034367 sponge, and its overexpression can inhibit the progression of medulloblastoma. Further experiments showed that the has-miR-17-3p inhibitor reversed the negative regulation of hsa_circ_034367 knockdown on medulloblastoma cell progression. In addition, DICER1 is the target of has-miR-17-3p, and its downregulation can inhibit the progression of medulloblastoma cells. Overexpression of DICER1 reversed the inhibitory effect of has-miR-17-3p on the progression of medulloblasto-

ma cells. Animal experiments showed that hsa_circ_034367 gene knockout can effectively inhibit cell apoptosis.

Conclusion: hsa_circ_034367 and DICER1 can inhibit medulloblastoma tumor growth. These data suggest that circRNA is a potential target for controlling the proliferation of SHH-type medulloblastoma.

Biography

Yafei Wang, M.D., studied Pediatric Neurosurgery at Xinhua Hospital, Shanghai Jiao Tong University. **Chenran Zhang**, M.D., Associate Chief Physician, Master's Advisor, is a member of the American Association of NeuroSurgeons (AANS) and the International Association of Pediatric Neurosurgery (ISPN).