Adenosylhomocysteinase

Dysregulated circRNAs in GBM tissues were screened out from Gene Expression Omnibus database. The expression of candidate circRNAs in GBM cells was measured by qRT-PCR. Loss-of-function assays, including colony formation assay, EdU assay, TUNEL assay, and flow cytometry analysis were conducted to determine the effects of circ-AHCY knockdown on GBM cell proliferation and apoptosis. Animal study was further used to prove the inhibitory effect of circ-AHCY silencing on GMB cell growth. Mechanistic experiments like luciferase reporter, RNA pull-down and RNA-binding protein immunoprecipitation (RIP) assays were performed to unveil the downstream molecular mechanism of circ-AHCY. Nanosight Nanoparticle Tracking Analysis (NTA) and PKH67 staining were applied to identify the existence of exosomes.

Results: Circ-AHCY was confirmed to be highly expressed in GBM cells. Circ-AHCY silencing suppressed GBM cell proliferation both in vitro and in vivo. Mechanistically, circ-AHCY activates Wnt/ β -catenin signaling pathway by sequestering miR-1294 to up-regulate MYC which activated CTNNB1 transcription. It was also found that circ-AHCY recruited EIF4A3 to stabilize TCF4 mRNA. Enhanced levels of TCF4 and β -catenin contributed to the stability of TCF4/ β -catenin complex. In turn, TCF4/ β -catenin complex strengthened the transcriptional activity of circ-AHCY. Exosomal circ-AHCY derived from GBM cells induced abnormal proliferation of normal human astrocytes (NHAs)¹.

1)

Li Y, Zheng X, Wang J, Sun M, Li D, Wang Z, Li J, Li Y, Liu Y. Exosomal circ-AHCY promotes glioblastoma cell growth via Wnt/β-catenin signaling pathway. Ann Clin Transl Neurol. 2023 May 7. doi: 10.1002/acn3.51743. Epub ahead of print. PMID: 37150844.

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