circASAP1

Acquired chemoresistance is a major challenge in the clinical treatment of glioblastoma (GBM). Circular RNAs have been verified to play a role in tumor chemoresistance. However, the underlying mechanisms remain unclear. The aim of s study was to elucidate the potential role and molecular mechanism of circASAP1 in temozolomide resistance of GBM.

Weiet al. analyzed circRNA alterations in recurrent GBM tissues relative to primary GBM through RNA sequencing. Real-time quantitative reverse transcription PCR (qRT-PCR) verified the expression of circASAP1 in tissues and cells. Knockdown and overexpressed plasmids were used to evaluate the effect of circASAP1 on GBM cell proliferation and temozolomide-induced apoptosis. Mechanistically, Fluorescence in situ hybridization, dual-luciferase reporter, and RNA immunoprecipitation assays were performed to confirm the regulatory network of circASAP1/miR-502-5p/NRAS. Intracranial tumors model was used to verify our findings in vivo.

Results: CircASAP1 expression was significantly up-regulated in recurrent GBM tissues and temozolomide-resistant cell lines. CircASAP1 overexpression enhanced GBM cell proliferation and temozolomide-resistance, which could reduced by circASAP1 knockdown. Further experiments revealed that circASAP1 increasd the expression of NRAS via sponging miR-502-5p. Moreover, circASAP1 depletion effectively restored the sensitivity of temozolomide-resistant xenografts to temozolomide treatment in vivo.

Conclusions: Our data demonstrate that circASAP1 exerts regulatory functions in GBM and that ceRNA-mediated microRNA sequestration might be a potential therapeutic strategy for GBM treatment [1)].

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Wei Y, Lu C, Zhou P, et al. EIF4A3-induced circular RNA ASAP1(circASAP1) promotes tumorigenesis and temozolomide resistance of glioblastoma via NRAS/MEK1/ERK1/2 signaling [published online ahead of print, 2020 Sep 14]. Neuro Oncol. 2020;noaa214. doi:10.1093/neuonc/noaa214