ADAR1

ADAR1, as a member of the ADAR family, plays an important role in cancer progression and chemotherapy resistance. However, the mechanism by which ADAR1 regulates GBM progression and TMZ resistance is still unclear.

Zhang et al. first constructed stable transfected strains in which ADAR1 was knocked down and overexpressed to investigate the effect of ADAR1 on the first-line glioma chemotherapy drug TMZ. Subsequently, they validated that ADAR1 induces autophagy activation and used autophagy inhibitors to suppress autophagy, demonstrating that ADAR1 enhances TMZ resistance through autophagy. They further knocked down p62 (SQSTM1) based on the overexpression of ADAR1, and the results showed that ADAR1 regulates selective autophagy through the p62 regulation. Finally, they demonstrated through mutations at both edited and nonedited sites that ADAR1 regulates selective autophagy in an edited-dependent way.

Further analysis showed that in the presence of TMZ, elevated ADAR1 promoted TMZ-induced autophagy activation. Further research revealed that ADAR1 enhances TMZ resistance through p62-mediated selective autophagy. Further, ADAR1 regulates selective autophagy in an edited-dependent way. Our results indicate a relationship between ADAR1 levels and the response of glioma patients to TMZ treatment.

They found that the expression of ADAR1 is upregulated in GBM and is associated with tumor grade and TMZ resistance. Elevated expression of ADAR1 predicts poor glioblastoma prognosis and promotes tumor growth in vivo or in vitro [1].

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Zhang Y, Guo H, Bu J, Wang W, Wang L, Liu Z, Qiu Y, Wang Q, Zhou L, Liu X, Ma L, Wei J. ADAR1 Promotes the Progression and Temozolomide Resistance of Glioma Through p62-Mediated Selective Autophagy. CNS Neurosci Ther. 2025 Jan;31(1):e70168. doi: 10.1111/cns.70168. PMID: 39825637.