

Glutaminase is an amidohydrolase enzyme that generates glutamate from glutamine. Glutaminase has tissue-specific isoenzymes. Glutaminase has an important role in glial cells. Glutaminase catalyzes the following reaction: $\text{Glutamine} + \text{H}_2\text{O} \rightarrow \text{glutamate} + \text{NH}_3$

Inhibiting [cancer metabolism](#) via [glutaminase](#) (GAC) is a promising strategy to disrupt [tumor progression](#). However, the mechanism regarding GAC acetylation remains largely unknown.

Mitochondrial protein isolation and glutaminase activity assay were used to examine GAC activity; RT-qPCR, western blot, sphere-formation, ALDH activity and tumor-initiating assays were performed to evaluate the alteration of cell stemness; Co-IP and rescuing experiments were constructed to explore the underlying mechanisms.

In this study, we demonstrated that GAC acetylation was a vital post-translational modification that inhibits GAC activity in glioma. We identified that GAC was deacetylated by HDAC4, a class II deacetylase. GAC acetylation stimulated the interaction between GAC and SIRT5, therefore promoting GAC ubiquitination and inhibiting GAC activity. Furthermore, GAC overexpression suppressed the stemness of glioma cells, which was rescued by deacetylation of GAC.

The findings reveal a novel mechanism of GAC regulation by acetylation and ubiquitination that participates in [glioma stemness](#) ¹⁾

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Xu G, Qu J, Zhang M. HDAC4-mediated deacetylation of glutaminase facilitates glioma stemness. *Curr Cancer Drug Targets*. 2023 Mar 29. doi: 10.2174/1568009623666230329123358. Epub ahead of print. PMID: 36999421.

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