Cancer metabolism

Cancer metabolism refers to the metabolic changes that occur in cancer cells, which enable them to grow and proliferate in a manner different from normal cells. Cancer cells have altered metabolism compared to normal cells, which provides them with a growth advantage and allows them to adapt to the harsh conditions of the tumor microenvironment.

One of the key metabolic alterations in cancer cells is the Warburg effect, which describes the increased glucose uptake and glycolysis that occurs in cancer cells, even in the presence of oxygen. This results in the production of lactate as a byproduct, which can further contribute to the acidification of the tumor microenvironment.

Other metabolic changes in cancer cells include alterations in lipid metabolism, increased glutamine uptake, and changes in mitochondrial function. These changes can contribute to the increased energy demands of cancer cells and the production of metabolites that support tumor growth and proliferation.

Understanding cancer metabolism is important for the development of new therapies that target specific metabolic pathways in cancer cells. This approach is known as metabolic therapy and is currently an area of active research.

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)]

1)

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.