論 文 要 旨

Targeting of the glutamine transporter SLC1A5 induces cellular senescence in clear cell renal cell carcinoma

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In recent years, cancer metabolism has attracted attention as a therapeutic target, and glutamine metabolism is considered one of the most important metabolic processes in cancer. Solute carrier family 1 member 5 (SLC1A5) is a sodium channel that functions as a glutamine transporter. In various cancer types, SLC1A5 gene expression is enhanced, and cancer cell growth is suppressed by inhibition of SLC1A5. However, the involvement of SLC1A5 in clear cell renal cell carcinoma (ccRCC) is unclear. Therefore, in this study, we evaluated the clinical importance of SLC1A5 in ccRCC using The Cancer Genome Atlas database. Our findings confirmed that SLC1A5 was a prognosis factor for poor survival in ccRCC. Furthermore, loss-of-function assays using small interfering RNAs or an SLC1A5 inhibitor (V9302) in human ccRCC cell lines (A498 and Caki1) showed that inhibition of SLC1A5 significantly suppressed tumor growth, invasion, and migration. Additionally, inhibition of SLC1A5 by V9302 in vivo significantly suppressed tumor growth, and the antitumor effects of SLC1A5 inhibition were related to cellular senescence. Our findings may improve our understanding of ccRCC and the development of new treatment strategies for ccRCC.