

C1GALT1 promotes invasive phenotypes of hepatocellular carcinoma cells by modulating integrin β 1 glycosylation and activity

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Abstract

Cancer cell invasion and metastasis are the primary causes of treatment failure and death in hepatocellular carcinoma (HCC). We previously reported that core 1 β 1,3-galactosyltransferase (C1GALT1) is frequently overexpressed in HCC tumors and its expression is associated with advanced tumor stage, metastasis, and poor survival. However, the underlying mechanisms of C1GALT1 in HCC malignancy remain unclear. In this study, we found that overexpression of C1GALT1 enhanced HCC cell adhesion to extracellular matrix (ECM) proteins, migration, and invasion, whereas RNAi-mediated knockdown of C1GALT1 suppressed these phenotypes. The promoting effect of C1GALT1 on the metastasis of HCC cells was demonstrated in a mouse xenograft model. Mechanistic investigations showed that the C1GALT1-enhanced phenotypic changes in HCC cells were significantly suppressed by anti-integrin β 1 blocking antibody. Moreover, C1GALT1 was able to modify O-glycans on integrin β 1 and regulate integrin β 1 activity as well as its downstream signaling. These results suggest that C1GALT1 could enhance HCC invasiveness through integrin β 1 and provide novel insights into the roles of O-glycosylation in HCC metastasis.

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