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C1GALT1 overexpression promotes the invasive behavior of colon cancer cells through modifying O-glycosylation of FGFR2

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Abstract

Core 1 β1,3-galactosyltransferase (C1GALT1) transfers galactose (Gal) to N-acetylgalactosamine (GalNAc) to form Galβ1,3GalNAc (T antigen). Aberrant O-glycans, such as T antigen, are commonly found in colorectal cancer. However, the role of C1GALT1 in colorectal cancer remains unclear. Here we showed that C1GALT1 was frequently overexpressed in colorectal tumors and is associated with poor survival. C1GALT1 overexpression promoted cell survival, migration, invasion, and sphere formation as well as tumor growth and metastasis of colon cancer cells. Conversely, knockdown of C1GALT1 with small interference (si) RNA was sufficient to suppress these malignant phenotypes in vitro and in vivo. Moreover, we are the first to show that fibroblast growth factor receptor (FGFR) 2 carried O-glycans in colon cancer cells. Mechanistic investigations showed that C1GALT1 modified the O-glycans on FGFR2 and enhanced bFGF-triggered activation of FGFR2 as well as increased bFGF-mediated malignant phenotypes. In addition, BGJ398, a selective inhibitor of FGFR, blocked the effects of C1GALT1. These findings suggest that C1GALT1 overexpression modifies O-glycans on FGFR2 and enhances its phosphorylation to promote the invasive behavior and cancer stem-like property in colon cancer cells, indicating a critical role of O-glycosylation in the pathogenesis of colorectal cancer.

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