The molecular chaperone Cosmc enhances malignant behaviors of colon cancer cells via activation of AKT and ERK

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Abstract
Expression of T antigen (Galbeta1,3GalNAc) is associated with enhanced metastatic potential and poor prognosis in colorectal cancer. Cosmc is a molecular chaperone required for the formation of an active T-synthase, which catalyzes the synthesis of T antigen. However, the expression and role of Cosmc in colorectal cancer are still unclear. Here, real-time PCR showed that overexpression of Cosmc mRNA in colorectal tumors compared with paired non-tumorous tissues was associated with increased American Joint Committee on Cancer (AJCC) tumor stage. Forced expression of Cosmc in HCT116 cells significantly increased T antigen expression and enhanced cell growth, migration, and invasion, which was associated with increased phosphorylation of focal adhesion kinase (FAK), ERK and AKT. These Cosmc-enhanced malignant phenotypes were significantly suppressed by specific inhibitor of MEK or PI3K. We also found that Cosmc overexpression increased tumor growth and decreased survival of tumor-bearing SCID mice. Conversely, knockdown of Cosmc with siRNA in SW480 cells decreased malignant behaviors and the signaling pathways, which were substantially reversed by constitutively active Akt or MEK. Taken together, these results suggest that Cosmc promotes malignant phenotypes of colon cancer cells mainly via activation of MEK/ERK and PI3K/AKT signaling pathways, and that Cosmc may serve as a potential target for colorectal cancer treatment.