SY-III-4 KITENIN CONTRIBUTES TO THE PROGRESSION OF COLON CANCER AS A NOVEL TARGET OF WNT PATHWAY

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Recently, we tried to identify proteins that interact with the cytoplasmic domain of KAI1 by yeast two-hybrid system on the assumption that the C-terminal region is important in regulating the functional characteristics of KAI1. We found a cDNA clone identified as the VANGL1 that interacted specifically with the C-terminal region of KAI1 and renamed it as KAI1 C-terminal interacting tetraspanin (KITENIN). We found that KITENIN is associated with promoting invasion and metastasis, and the interaction of two tetraspanins, KITENIN and KAI1, affects cellular motility and invasion and thereby regulates tumor formation and metastasis. There was a positive correlation between the expression of KITENIN and the presence of distant metastasis, indicating that KITENIN can function as a metastasis-inducing gene. We also examined the transcriptional regulation of KITENIN in the colon cancer cells and tried to provide a possible explanation for the metastasis-enhancing nature of KITENIN. We found that KITENIN is a novel target gene of b-catenin/TCF4 pathway. KITENIN-transfected intestinal epithelial cells represented more enhanced cell migration and invasion but less anoikis than parent cells. In addition, KITENIN was highly expressed in the whole tumor portion of human colon cancer tissues that showed adenocarcinomatous changes. These results support a key role of KITENIN for tumor progression and metastasis by mutational deregulation of the Wnt cascade in colon cancer.

Key Words: KITENIN, Tumor progression, Wnt