Axis inhibition protein 1 (AXIN1) is a negative regulator of Wnt/beta-catenin signaling via regulating the level of beta-catenin. However, the role of AXIN1 in the tumorigenesis and progression of hepatitis B virus (HBV)-related hepatocellular carcinoma (HCC) is less clear. PCR sequence analysis, immunohistochemistry, and Western blot were performed on 22 HBV-related HCC samples and corresponding nontumor liver tissues to detect variants in AXIN1 gene and the expression level of AXIN1. Human hepatoma cell lines SNU475 and SNU423 were transfected with pCDNA3.1-AXIN1-myc or AXIN1 G425S-myc mutant. The growth curve and apoptosis rate of cell lines, phosphorylation of beta-catenin, and cell cycle regulatory proteins depending on beta-catenin transcriptional activity were detected. We identified four mutations of AXIN1 in 22 primary HBV-related HCCs and demonstrated a lower expression of AXIN1 in HBV-related HCC tissues than that in paired adjacent nontumor tissues. Overexpression of AXIN1 wild-type but not AXIN1 mutant inhibited the growth of HCC cell lines, accelerated their apoptosis, and negatively regulated beta-catenin-dependent transcriptional activity. Our study revealed that alterations of AXIN1 were involved in HBV-related HCC. Overexpression of AXIN1 but not AXIN1 mutant negatively regulated beta-catenin-dependent transcriptional activity and downregulated the level of cell cycle regulatory proteins, suggesting that AXIN1 may be a potential target for gene therapy of primary HCC [1)].

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Li J, Quan H, Liu Q, Si Z, He Z, Qi H. Alterations of axis inhibition protein 1 (AXIN1) in hepatitis B virus-related hepatocellular carcinoma and overexpression of AXIN1 induces apoptosis in hepatocellular cancer cells. Oncol Res. 2013;20(7):281-8. PubMed PMID: 23879168.