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HBV regulates the alternative splicing of KIAA0101 in hepatocellular carcinoma via suppressing SRSF2**Lijuan Liu, Youyi Liu, Yan Zhou, Ping Zhou and Fan Zhu**
Wuhan University, China

Hepatocellular carcinoma (HCC) is one of the most-deadly human cancers. Approximately half of HCC cases are associated with chronic hepatitis-B virus (HBV) infection. Our previous work demonstrated that transcript variant (tv) 1 of KIAA0101, which is overexpressed in HCC, prevented apoptosis after Doxorubicin treatment through inhibiting p53. In this study, we found aberrant expression of KIAA0101 tv1 in HBV-related HCC (HBV-HCC) compared with non-virus-related HCC (non-virus HCC). HBV increased the alternative splicing (AS) of KIAA0101 tv1 in HCC cells. Splicing minigene reporter assay revealed that HBV promoted KIAA0101 exon 3 inclusion, additionally, HBV down-regulated serine/arginine-rich splicing factor-2 (SRSF2), which inhibited the inclusion of KIAA0101 exon 3 through a putative cis-element GATTTCCTG. These results implicated that HBV regulated aberrant AS of KIAA0101 through suppression of SRSF2 function via a motif on KIAA0101 exon 3 in HCC. Moreover, our studies showed that KIAA0101 tv2 was overexpressed in the adjacent non-tumorous tissues (NTs) compared with HCC tissues. Interestingly, unlike KIAA0101 tv1, KIAA0101 tv2 failed to promote NIH3T3 cell growth, colony formation, tumor xenografts, motility and metastasis, showing the opposite function of tv1. Furthermore, KIAA0101 tv2 restrained HCC progression partially by down-regulating KIAA0101 tv1. KIAA0101 tv2 could increase the activity of p53 via competing with KIAA0101 tv1 for binding to P53. HBV could induce HCC through increasing the splicing of KIAA0101 tv1 and decreasing the expression levels of KIAA0101 tv2 via suppression of SRSF2. KIAA0101 tv2 exhibits the property of tumor-suppressor and acts as a negative regulator of oncogenic KIAA0101 tv1. KIAA0101 tv2 is likely to be a promising strategy to develop novel HCC therapeutic drug.

Biography

Lijuan Liu has her expertise in study of the molecular mechanisms of aberrant alternative splicing in hepatitis-B virus-associated hepato-carcinogenesis. Her research explores the role of HBV on the aberrant regulation of host genes' AS in HBV-associated HCC.

liuli-juan@163.com

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