catenin mutations are associated with a subset of low stage hepatocellular carcinoma negative for hepatitis B virus and with favorable prognosis.

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摘要

Abstract

To better understand the role of ß-catenin mutation in hepatocellular carcinoma (HCC), we correlated the gene mutation with hepatitis virus B (HBV) and hepatitis virus C (HCV) status and the clinicopathological features in 366 patients with resected primary unifocal HCC. ß-Catenin mutations were also analyzed in 55 patients with multifocal HCC (68 tumors). Of the whole series, 57 (13.1%) of 434 tumors examined had ß-catenin mutations, 34 occurred at the serine/threonine residues of the GSK-3ß region of ß-catenin. Outside the GSK-3ß phosphorylation site, codons 32 and 34 were two mutational hot spots (17 tumors). The non-HBV-related HCC that was predominantly HCV related had a higher frequency of mutation ($P < 0.00001$) and more frequent mutations at codon 45 than HBV-related HCC. HBV-related HCC had a younger mean age ($P < 0.00001$), and higher male-to-female ratio ($P < 0.003$) and positive familial history of HCC ($P < 0.014$). Among 366 unifocal HCCs selected for clinicopathological analysis, ß-catenin mutations were associated with grade I ($P = 0.005$) and stage I and II HCC ($P < 0.0001$), and a better 5-year survival rate ($P = 0.00003$). These findings suggest mechanisms for ß-catenin mutations differ between HBV-related and non-HBV-related HCCs, and that ß-catenin mutation is a favorable prognostic factor related to low stage. ß-Catenin mutation was associated with nuclear expression of the protein ($P < 0.00001$), but we failed to detect point or large fragment deletion mutation in 39 HCCs with nuclear ß-catenin expression, presumably wild-type protein. HCCs expressing mutant nuclear ß-catenin had a better 5-year survival rate ($P < 0.007$), suggesting that mutant and wild-type nuclear ß-catenin proteins are not functionally equivalent and deserve more studies for further clarification.