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A variant in microRNA-196a2 is associated with susceptibility to hepatocellular carcinoma in Chinese patients with cirrhosis

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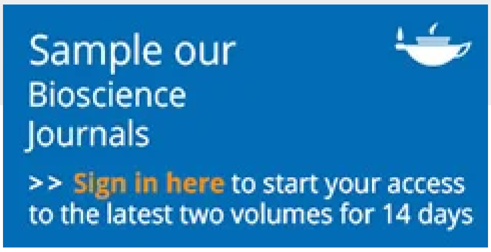

Abstract

Aims: Cirrhosis is an important risk factor for hepatocellular carcinoma (HCC) in China, while little is known of the genetic susceptibility to hepatocarcinogenesis. Traditional approaches to identification of novel genetic predisposition genes have focused on protein encoding genes. There is evidence to suggest that microRNAs (miRNA) may play an important role in tumorigenesis. Recent studies have implicated that the rs11614913 SNP in miR-196a2 may be associated with susceptibility to lung cancer, congenital heart disease, breast cancer, as well as reduced survival in non-small cell lung cancer. This study aims to assess whether this functional polymorphism can influence susceptibility to and the progression of cirrhosis-related HCC.

Methods: 532 patients with hepatic cirrhosis (310 patients with HCC and 222 patients without HCC) were enrolled. DNA was extracted from blood specimens, and miR-196a2 polymorphism was genotyped by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP). In addition, tumour tissues of liver (n=59) were obtained from the studied HCC patients for measurement of miR-196a expression levels.

Results: The frequency of the CC genotype among HCC patients was higher than that in the control group, implying that the cirrhotic patients with the CC genotype or C allele containing genotypes (CT and CC) may have a higher risk of HCC. However, in a subsequent analysis of the association between this polymorphism and clinicopathological characteristics, there was an association between rs11614913 genotype and tumour size ($p=0.046$), but not with tumour number, grade, stage, invasiveness or Child-Pugh grade. In a genotype-phenotype correlation analysis using 59 tumour tissues of liver, rs11614913 CC or carrying at least one C allele was associated with significantly increased mature miR-196a expression ($p=0.006$ or $= 0.002$).

Conclusions: Our results suggest, for the first time, that miR-196a2 polymorphism may contribute to cirrhosis–related HCC susceptibility in Chinese patients through influencing mature miR-196a expression.

Key words:

Cirrhosis hepatocellular carcinoma MiR-196a2 single nucleotide polymorphism

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