Mechanisms of Hepatitis B Surface Protein-Related Hepatocarcinogenesis

Background

Chronic HBV infection is strongly associated with the development of hepatocellular carcinoma, but the molecular mechanisms underlying HBV-induced tumourigenesis remain largely debated. HBV DNA are frequently integrated into host genome. However, in contrast to the woodchuck model, in which specific HBV-DNA integration is detectable in most cases, insertional (in-) activation of cellular genes seems to be a rare event in human.

Reseach frontiers

The recent discovery of trans-activation functions exerted by truncated and mutated preS2/S [the LHBs and truncated MHBs] proteins supports the notion that transactivation of cellular gene expression could be relevant to hepatocarcinogenesis. This review will discuss the molecular mechanisms that trans-activation by mutated preS2/S is a possible mechanism for HBV-associated carcinogenesis.

Application

Serum pre-S2 deletion mutants and type II “Ground Glass” hepatocytes might be applied in the early diagnosis of HBV-related HCC as novel biomarkers. In addition, treatments to inhibit HBsAg and damage secondary to HBsAg or the preS/S mutants include antivirals and antioxidants should be comprehensive.

Answering Reviewers*

Thanks a lot for the reviews’s advice!

1 The reviewers suggest the title, Mechanisms of Hepatitis B Surface Protein-Related Hepatocarcinogenesis which shows the major important point of the review. Our primary intention is to fully understand HBV surface proteins in HCC, including the mechanism of hepatocarcinogenesis, clinical association between hepatitis B surface proteins and HCC, epidemiology of pre-S mutants, and measures to treat HBV surface proteins and damage secondary to the surface proteins.

2 Although epidemiological studies have provided overwhelming evidence for a causal role of CHB infection in HCC development, studies of HBV-induced tumorigenesis are widely debated. HBV-DNA integration, similar to the HBx protein and surface proteins, has been studied extensively in hepatocarcinogenesis. However, different opinion indicated that most of HBV

DNA integration events are not associated with hepatocarcinogenesis[Jiang S, Yang Z, Li W, Li X, Wang Y, Zhang J, Xu C, Chen PJ, Hou J, McCrae MA, Chen X, Zhuang H, Lu F.Re-evaluation of the carcinogenic significance of hepatitis B virus integration in hepatocarcinogenesis.

PLoS One. 2012;7(9): e40363. [PMID:22962577 DOI: 10.1371/journal.pone.0040363]. Both HBx and HBs (mutant) proteins are designated “viral oncoproteins” which are important in hepatocarcinogenesis.

3 The review discussed trans-activation by mutated preS2/S. Only the carboxy-terminal truncation of LHBs or MHBs has trans-activating properties. Trans-activation by mutated preS2/S plays an important role in HBV-associated carcinogenesis. The preS/S mutants at different sites have transactivating effects to trigger a protein kinase C (PKC)-dependent signal cascade, and result in the activation of transcription factors for HBV-associated carcinogenesis.