Hepatitis B Virus Large Surface Protein And Replication In Viral Replication And Hepatocellular Carcinoma: Developments In Diagnostics And Clinical Applications

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Liver cancer caused by chronic hepatitis B (CHB) infection is among the major public health issues in Taiwan and many countries in the world. One-third of the world's population (approximately 2 billion) have been infected with hepatitis B virus (HBV), of which 350 million have progressed to chronic carriers and are in high risks to hepatocellular carcinoma (HCC). Long-term and continuous follow up of CHB with HCC high-risk biomarkers is very important. In addition, it is also an important issue to identify prognostic biomarkers for patients after HCC surgery. We found that the HBV surface gene (HBS) pre-S2 mutant induces oxidative damage and mutation of host cell genes, leading to genomic instability, which in turn leads to HCC. In recent years, we conducted clinical research and developed the Pre-S gene chip to screen for pre-S mutants of hepatitis B carriers, and established high-risk biomarkers for HCC recurrence. We found that the HBS pre-S mutants provoke the genetic instability of hepatocytes and activates the carcinogenic mechanism. The clinical study of HCC patients in Cheng-Kung Hospital showed that the ratio of serum pre-S2 mutation oncogene was closely related to the recurrence and prognosis of HCC. The higher the ratio of pre-S2 mutants, the higher the probability of recurrence. Therefore, the pre-S2 mutant oncogene is a high-risk biomarker for recurrence, and can be potentially used to evaluate the relative risk of recurrence of HCC patients. In addition, our laboratory in-house developed monoclonal antibodies against the HBV large surface protein (LHBS). We found that LHBS is highly expressed in HCC tissues and plays a key role in HCC development. In order to delineate the replication mechanism of HBV, we have also developed a high-sensitivity digital PCR technology for detection of the key viral replication product cccDNA through an industrial-academic cooperation. Drug screening for viral cccDNA inhibitors is underway.

Fig. 1 Left: Expression of the HBV large surface protein in HCC tissues. Right: the front cover of the journal Hepatology showing the article title of our study.