PREDICTING RISK OF HEPATOCELLULAR CARCINOMA FOR PATIENTS WITH CHRONIC HEPATITIS B USING SERUM LEVELS OF SPLICED HEPATITIS B VIRUS DNA

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Introduction:

Over 257 million people live with chronic hepatitis B, resulting in up to 880,000 deaths annually due to cirrhosis and liver cancer (hepatocellular carcinoma, HCC). Identifying mechanisms by which HBV causes liver cancer is of paramount importance. We have previously shown that HBV splice variants were strongly associated with liver cancer[1]. The purpose of the current study was to validate these findings using a large international cohort of patients with HBV-mediated liver cancer, from the REVEAL[2] study in Taiwan

Methods:

HBV DNA in serum was purified from over 150 patients with liver cancer and 370 control patients who had chronic HBV but had not developed liver cancer. The ratio of splice variant to wild-type HBV was quantified by real time PCR and associations between the relative abundance of splice variants and liver cancer was determined by univariate and multivariate analysis.

Results:

Quantitative real time PCR was performed for splice (spHBV) and wild-type HBV DNA on over 600 samples. After adjustment for known HCC-related risk factors, subjects with spliced HBV DNA level >10% were at least 3 times more likely to develop HCC than patients with lower levels of splice variants. For patients with secreted spHBV of >20%, the likelihood increased to **23.3 times more**. In most HCC patients with elevated spHBV levels, splice levels increased in the 5 years prior to HCC diagnosis.

Conclusion:

Our previous pilot study suggested that the secretion of splice HBV variants into the blood compartment was strongly associated with liver cancer. We have now validated this finding utilising the highly characterised REVEAL Taiwanese cohort. The striking finding that HBV infected subjects were 23 times more likely to develop liver cancer if splice variants formed at least 20% of the secreted viral pool suggests we have identified a novel biomarker of HCC in this setting.