

### **Please Notify:**

- I am submitting the Word format of the manuscript
- Manuscript have been carefully revised by the authors
- The changes have been highlighted through track changes format
- Comments section on Background, Innovations and Breakthrough, Research Frontier, Applications, Terminology and Peer Review have been included
- I am submitting the Signed Copyright Forms from all authors

**Response to the Reviewers:** We like to thank the reviewers for their comments.

**Reviewer's code:** 02860797

### **Response:**

In this retrospective analysis, we included only treatment-naïve patients when comparing the intrahepatic HBsAg and HBcAg distributions between HBeAg positive and negative patients with chronic hepatitis B without HCC. Among those with HCC, the majority of the patients were treated with antiviral therapy at the time of cancer diagnosis. Since a proportion of those patients were referred to our center for HCC management, we did not have their complete hepatitis B history prior to the development of HCC. The key observation, however, remains true despite this limitation. We observed presence of viral antigens in tumor tissues but not in the adjacent non-tumor tissues in a relatively high percentage of patients who were documented to have undetectable HBV DNA in serum at time of biopsy. We concluded that there was a difference in the kinetics of therapy-induced viral clearance in tumor and non-tumor liver tissues. In a prospective study, one may be able to further examine this difference in viral kinetics taking into account therapy duration and potency. We emphasized this as a limitation of the retrospective study.

**Reviewer's code:** 01560036

### **Response:**

We went through the entire manuscript for language polishing and have removed the misprints in text and references as far as possible.