Reply to reviewer's comments

1) However, I would like to mention that, as the progression of liver disease in HBV infection is fostered by active virus replication which in turn is reflected by serum HBV DNA high levels. I wonder if the author can perform an epidemiological investigation of this mutation and the relationship to the HBV viral load in his group of patients (the chronic and the HCC patients too) may be by review their case record and the progression of level of viremia??. Given that the HBV DNA load reflects the physiological outcome of the viral infection and thus aggravation of the infection from chronic stage to HCC development it will be interesting to investigate the viral load…

- **Of 3 HCC related mutation types identified in this study (rt80, rt139, and rt204), only a rt80 mutation was significantly related to increased HBV replication. So, we added the Table 6 showing comparison of clinical features between patients with or without L80I and the following sentence in the discussion section (line 383 to 386). "Notably, our findings that L80I was combined with the rtM204I/V mutations in all 5 patients (data not shown) and L80I was also significantly related to increased HBV replication (Table 6) suggested that this mutation might play a role in compensating for the defective replication of rtM204I/V."**

2) I had some difficulties in reading the table 3 and I wonder if the author would be able to present it better with clear version and well organized.

- **According to reviewer's comment, we changed Table 3 into novel one**