In this study, Miura et al. investigate the correlation between FGF19 expression and the clinical parameters for prognosis evaluation in HCCs. mRNA expression of FGF19 and its receptor FGFR4 were detected in 40 human HCC samples compared with their background counterparts. The correlation of FGF19 mRNA expression in tissues and clinic parameters was analyzed. In addition, FGF19 expression in 10 HCC cell lines and their supernatants were also measured by RT-PCR, IH and ELISA respectively. Functional studies (proliferation, apoptosis and invasion) were performed by up-regulating (FGF19 recombinant protein) or down-regulating FGF19 (FGF19 siRNA). Based on their findings, the authors propose that FGF19 expression is significantly up-regulated in HCCs and this higher expression correlates with poor prognosis.

Major points:

1. The authors demonstrate that FGF19 mRNA is up-regulated in 40 resected HCC tissue samples and that there is a difference in FGF19 serum levels in 29 patients with HCC at pre- and postoperative period. This suggests that FGF19 could be used as a novel serum biomarker for HCC. It is unclear as to whether the patients consisting of the group of 40 HCC tissues are different patients from the 29 where serum was examined. If they are not the same, serum FGF19 should be examined in those 40 patients where HCC tissue were taken to determine if corresponding serum levels are also elevated. Also, are there differences in FGF19 serum level between HCC patients and health controls?

2. The authors state that “No significant correlation was found …… any of the general clinicopathological parameters, such as tumor size, tumor multiplicity, vascular invasion, histological grade, or histological type”(Page 12). However, in Table 1, there appears to be a significant correlation between the pathological stage and FGF19 mRNA expression (The P value is less 0.05 which was stated as the presence of a statistically significant difference in Page 11), so the statement is not accurate.

3. The results of RT-PCR show that JHH7 and Huh7 cells have the highest expression of FGF19, and HLE and HLF cells have the lowest expression of FGF19. However, the results of immunohistochemistry were inconsistent with the results of RT-PCR, showing the highest expression of FGF19 in HLF and relatively lower level in JHH7 and Huh7 cells. It will be clearer to present protein quantification by western blot than by Immunohistochemistry. In addition, to demonstrate higher expression of FGF19 in HCC cell lines, the comparison with
normal primary hepatocytes should be performed.

4. In the functional studies, the authors stated “the proliferation of all HCC cells examined increased significantly upon addition of FGF19 recombinant protein at concentrations of 0.01 to 10ng/ml over 48-96h (Fig. 4; n=12, P < 0.05)”. However, in Figure 4, only one time point results was presented. To show the proliferation curve, all time points should be represented. Besides, did all concentrations have the significance in proliferation assay? What is “n=12” for in Fig.4, Fig. 5A, Fig. 6E, Fig 6F? Were these experiments repeated 12 times?

Minor points
1. In Figure3C and 3E, what do the closed rectangles indicate? (no corresponding texts or figure legends)?
2. The authors state in discussion “RNA interference (RNAi) is a new technique…… ”. This should be deleted since RNAi technique is widely used and a general method for gene knockdown.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

'I declare that I have no competing interests'