The major aim of this study was to investigate the role of 14-3-3# in HCC. Analysis of a large sample collection revealed abundant expression of 14-3-3# in more than 70% of HCC patients. 14-3-3# was found to induce HSF-1#/HSP70, and intervention with HSP70 was shown to reduce cell migration. Inactivation of #-catenin abrogated 14-3-3# mediated upregulation of HSF-1#/HSP 70 expression suggesting a regulatory role of the canonical Wnt/#-catenin signaling in the 14-3-3#/HSF-1#/HSP 70 axis.

Overall, the study shows insights into the role of 14-3-3# in HCC. The authors made some efforts to describe the 14-3-3#/HSF-1/HSP 70 expression in primary HCC and to correlate it with clinicopathological parameters. The molecular link between 14-3-3#, HSP70 and #-catenin and its function in cell migration remains to be elucidated. Some data are inconsistent and must be better described. Unfortunately the text contains a number of mistakes concerning grammar and syntax which do not ease the reviewing process and give the whole manuscript a negligent appearance. The following points must be addressed for clarification and improvement of the manuscript.

Major Compulsory Revisions
1. Results, p9: “... increased 14-3-3# expression was significantly associated with surgical margin (P=0.008), capsular formation (P=0.028) and ...” The implications of these findings must be explained.
2. Results, p9 and p11: the term “marginal significance” is very misleading and must be deleted as it is a range without statistical significance.
3. Results, p10: the expression profiling must be made available in supplementary data.
4. Fig 2A: a Western blot is shown with numbered lanes from 1 to 4. I assume these numbers account for different clones of Huh7 cells overexpressing either 14-3-3# or a control construct. However, this is nowhere described properly.
5. Fig 2B: show HSF-1 and HSP70 expression by qPCR for all 4 controls and 4 cell lines overexpressing 14-3-3#.
6. Fig 2: it is nowhere explained which clones were used for the further analysis (Fig 2B / C / D / E).
7. Fig 4: it can only be assumed that overexpression or knockdown cells are
Huh7, as this is nowhere stated. Fig 4B must be wrong as it shows an induction of migration due to 14-3-3# knockdown, which is the opposite of what the text says. Interestingly it contains 2 variants of knockdown and control that are supposedly significantly different from one another, however, again it is nowhere stated what these might be.

8. Same is true for Fig 4D.

9. Fig 5 tries to explain the dependency of HSF-1 expression on the presence of #-catenin. Now interestingly in the case of 14-3-3# overexpression and strongly elevated HSF-1 protein levels, the knockdown of #-catenin causes complete loss of HSF-1. However, knockdown of #-catenin does not significantly change HSF-1 expression in control cells. This is a striking discrepancy and questions the role of #-catenin in the expression of HSF-1 and therefore clearly needs to be addressed by the authors.

10. The effect of intervention with #-catenin signaling (#-catenin siRNA) should be shown on the migration of cells used in Fig 5 (Huh7 cells overexpressing 14-3-3# and SK-Hep1).

11. Discussion: The discrepancy between effects on cell migration and invasion must be discussed. The activation of the HSF-1 promoter by #-catenin should be considered (putative TCF/Lef binding sites?).

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

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