

Peer Review File

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Reviewer A

Comment 1: Please revise formatting and font throughout as it sometimes differs, and provide a citation for line 81-82. Please check the typical errors such as no spacing between one figure number and the other etc.. e.g. figure 8A,8B versus 8A, 8B.

Reply 1: We have revised formatting and font throughout, and provided a citation for line 81-82 (see Page 3, line 84). We have modified the typical errors such as no spacing between one figure number.

Changes in the text: line 84;

Comment 2: The introduction is a bit lacking, and in need for some literature review for example lines 431-436 should be adapted and edited into in for more context and an authentication of the rationale thus setting the tone moving forward.

Reply 2: We added some literature review (see Page 14, line 440) and have modified our text as advised (see Page 13, line 442-440).

Changes in the text: line 442-450

Comment 3: For the methods the way the patients are jotted down need to be clarified, as a reader I had to go up and down a few times to figure out that you had 180 patients, and the assumption primarily indicated that this was an Insilco analysis based on a repository but then having gone down to the IHC, I had to go back up and check it so I suggest you review it for cohesiveness and clarity.

Reply 3: We apologize for any confusion it may have caused and have adjusted the order of subheadings (see Page 8-9, line 256-277)

Changes in the text: line 256-277

Comment 4: 499: In our investigation, IHC experiments confirmed that MRGBP 500 stimulates the malignant progression of HCC. These results align with the findings 501 from bioinformatic analyses and previous studies. (What previous studies please specify.

Reply 4: The previous studies have been mentioned above. We regret any inconvenience this may have caused and We have modified our text (see Page 16, line 510)

Changes in the text: line 510

Comment 5: Your discussion is in dire need of some critical discussion, you do cite literature however it is in no way critical and your voice is focused on interpreting your results rather than associating them and evaluating them against the literature please try to address this your work seems top notch and your ideas are excellent.

Reply 5: We have carefully reviewed our discussion and We have modified our text as advised (see Page 14, line 442-450, 514-521)

Changes in the text: line 442-450, 514-521

Comment 6: Your conclusion should highlight the main findings and provide a recommendation of what to do moving forward please check it. The graphs and figures are excellent overall quite clear and interesting and labelled in a manner that even smaller ones you can easily check the terms

Reply 6: Your suggestion is very relevant and We have modified our text as advised (see Page 16, line 525-536). Thank you for acknowledging our work

Changes in the text: line 525-536

Reviewer B

Comment 1: First, I suggest the authors to indicate the prognosis outcome in the title such as OS

Reply 1: We tried to modified our title as advised (see Page 1, line 1-2)

Changes in the text: line 1-2

Comment 2: Second, the abstract needs some revisions. The background did not describe the knowledge gap on and the potential clinical significance of this research focus. The methods need to briefly describe the clinical samples, prognosis outcomes, the generation of training and validation samples, and how the predictive accuracy was examined. The results need to describe the clinical predictors in the prediction model and AUC values to denote its accuracy. The authors need to quantify the findings in this part including the survival rates and accurate P values. The conclusion needs comments for the limitations of this study and detailed suggestions for the clinical implications of the findings

Reply 2: Sincerely thank you for pointing out our shortcomings. We have modified our abstract as advised (see Page 2-3, line 47-74)

Changes in the text: line 47-74

Comment 3: Third, in the introduction of the main text, it is necessary have a detailed review on the prognostic biomarkers and prognosis prediction models in HCC, analyze their limitations and predictive accuracy, and, importantly, analyze why CR is important. The authors need to analyze the limited studies on CR in HCC and analyze their limitations. The authors also need to explain why the addition of clinical factors in the prediction model is important because their model is based on CR and clinical variables. In the methodology, the authors need to describe the research design, the prognosis outcome, the clinical sample in the dataset, and statistical methods for assessing the predictive accuracy, as well as the threshold C-index value for a good predictive model

Reply 3: We have carefully reviewed the main text and have modified our text as advised (see Page 3, line 103-105, 117-130)

Changes in the text: line 103-105, 117-130

Comment 4: Finally, please consider to cite several related papers: 1. Ji P, Wang H, Cheng Y, Liang S. Prognostic prediction and gene regulation network of EIF2S2 in hepatocellular carcinoma based on data mining. *J Gastrointest Oncol* 2021;12(6):3061-3078. doi:

10.21037/jgo-21-748. 2. Luan M, Tian X, Zhang D, Sun X, Jiang M, Duan Y, Sun C, Si H. Identifying the potential regulators of neutrophils recruitment in hepatocellular carcinoma using bioinformatics method. *Transl Cancer Res* 2021;10(2):724-737. doi: 10.21037/tcr-20-2714. 3. Lim JJ, Chow EKH, Toh TB. Eph receptor B2 (EPHB2) regulates cancer stem cell-like properties in hepatocellular carcinoma. *Stem Cell Investig* 2022;9:5

Reply 4: We have cited these related papers (see Page 3-4, line 94-102)

Changes in the text: line 94-102