Peer Review File

Reviewer A:

It is an interesting topic which tell us cancer-associated fibroblasts can enhance the chemoresistance of CD73+ hepatocellular carcinoma cancer cells via HGF-Met-ERK1/2 pathway. The novelty for this hypothesis is CD73+ HCC.

1.English is poor and editing is mandatory.

We apologize for the poor language of our manuscript. We have now worked on both language and readability and have also involved the highly qualified native English-speaking editors at AME Publishing Company for language corrections. We really hope that the flow and language level have been substantially improved.

2.All images need to do the quantitative analysis.

We checked our pictures in detail and performed a quantitative analysis on all the figures, especially the WB, and attached the additional figures next to the WB pictures.

3. Although only 25 cases are not strong enough to show the relationship in the clinical level, the authors should give the basic information of these 25 cases.

For the basic information of 25 clinical cases, we have added in the supplementary material as Table S1, thank you for pointing out.

4. The abstract must be rewritten, especially the method part.

We fixed incorrect syntax errors and especially rewritten the method part in the abstract.

5. It would be appreciated that authors could provide a picture to show the whole story of this hypothesis.

We have provided a picture based on our ideas and hypothesis to show the whole story, named Figure7.

6. Introduction part cannot display results.

Thanks for your suggestion, we have removed the results from the introduction part and rewritten the introduction.

Reviewer B:

This study provides novel information that CAF-secreted HGF promotes CD73 expression via MET/ERK1/2 pathway. Subsequently, CD73 contributes to chemoresistance, stemness properties and tumorigenicity of HCC.

1. The background of HCC samples for CAFs and NFs isolation should be provided. If these patients have hepatitis, the fibroblasts in normal tissues are activated. Moreover, hepatic stellate cells rather than portal fibroblasts are recognized as the main source of CAFs. Thus, author should identify which cell type is isolated.

We have provided the background of isolated CAFs and NFs. The NFs were extracted from normal liver tissue from patients with hepatic hemangioma, and without hepatitis. The basic information of patients was summarized in the supplementary TableS1. Patient whose Number 0999159 was extracted as NFs, and Number 0998904 was extracted as CAFs. The extraction of CAFs was strictly in accordance with the methods described in the literature(methods part in the article), and verified by CAFs marker, aSMA and Vimentin.

2. According to previous study (J Hematol Oncol. 2019 Apr 11;12(1):37. doi: 10.1186/s13045-019-0724-7.), Hep3B cells shows the relative highest level of CD73, whereas HepG2 cells shows the relative lowest level of CD73 among seven HCC cell lines. In this study, the basal levels of CD73 in both Hep3B and HepG2 are weak. How to explain?

Thanks for your questions. I also noticed this article and felt very strange, but after repeating it several times, the results are still the same, including the results of PCR and flow cytometry, I think it may be due to different growth environment or cells with different passages, or there are maybe other reasons, thus I can't repeat their results.

3. All WB need at least three independent repeats and statistical analysis.

Thank you for your suggestion, all WB results have been repeated independently at least 3 times and statistical analysis has been performed, the corresponding results are presented in figures.

4. Scale bars are necessary for figure 5E and 6F.

We have added the scale bars to the figure5E and figure6F according to your requirements. Thank you for your reminder.