Reviewer’s report

Title: The role of c-Src in the invasion and metastasis of hepatocellular carcinoma cells induced by association of cell surface GRP78 with activated alpha2M

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Reviewer: Po-Li Wei

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Major Compulsory Revisions

This study demonstrated that #2M* may enhance the cell invasion by the increase of the surface GRP78 but not influence the expression of total GRP78. Cell surface GRP78 could interact with c-SRC to promote the invasion on HCC cells. Further surface GRP78 with #2M* facilitates the interaction of EGFR and c-SRC and caused the phosphorylated EGFR to promote the invasion of HCC. The study is interesting. However, there are many major concerns for this study. The description for the results should be more precisely. In addition, the resolution of image is needed to be improved. Some control groups also needed to perform.

1. Fig1e-g, please show the results w/o #2M*.
2. Lune 281 what’s mean “parallel”. The description may need more specific and clear.
3. The resolution for Fig2e is not good. It needs to be performed by confocal microscope. The image is not clear and background is very high. In addition, the author didn’t describe what’s mean for “WAG”?
4. Fig3a, the signal in 60kD by probed anti-p-Tyr should not be p-SRC (Line300). There is other possibility. The statement needs to be rewritten.
5. Fig3: The pull down assay showed GRP78 can form the complex with p-c-SRC. It is hard to realize that the complex is formed by surface GRP78 or other form GRP78 with p-SRC?
6. Fig4b, What’s the pattern for surface GRP78 after PP2 treatment? It needed to show the results here.
7. Fig4. How about the effect in PLC cells?
8. Fig5. How about the staining pattern of GRP78? Is it possible double staining for GRP78 and paxillin re-distribution? In addition, the authors needed to show more clearly for the formation of invadopodia.
9. Fig6. The results need to be quantified. Fig6b-d: Lacked the PP2 only results.
10. Fig7. The authors needed to show the staining pattern for adjacent normal control. The image is hard to distinguish surface GRP78 or cytosolic GRP78.

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' below