Reviewer's report

Title: Grp78 promotes the invasion of hepatocellular carcinoma

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Reviewer: Jin-zhang Zeng

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Major Comments:
1. The expression of Grp78 in HCC. It is not clear that the immunostaining of Grp7 protein is associated tumor grades as indicated in Fig. 1. HE staining for indication of tumor grades should be provided. In addition, it is better to include staining of both tumor and the corresponding nontumor tissues in one picture. Western blotting analysis should be also performed.

2. The SMMC7721 was the only cell line for mechanistic study. However, this cell line endogenously expresses high level of Grp78 (Fig. 2A). They should conduct experiments in various HCC cell lines to see whether Grp78 expression levels are associated with tumor invasive phenotypes. Using those cell lines with low or undetectable of Grp78 in their transfections will help to demonstrate the oncogenic activity of Grp78, while knockingdown Grp78 in those cell lines with high level of Grp78 will contribute to the conclusion.

3. Transwell assay in Fig. 2C. They should also provide the staining results.

4. The Grp78-transfected cells did not show a significant increased spreading feature (Fig. 3).

5. The phospho-FAK staining should be costained with anti-Grp78 to compare their association (Fig. 4A). Grp78 transfection did not obviously increase the levels of phosphor-FAK (Fig. 4B). These experiments need to be repeated.

Level of interest: An article of insufficient interest to warrant publication in a scientific/medical journal

Quality of written English: Not suitable for publication unless extensively edited

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