Reviewer’s report

Title: Cancer stem-like sphere cells induced from de-differentiated hepatocellular carcinoma-derived cell lines possess the resistance to anti-cancer drugs

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Reviewer: José Manuel García-Heredia

Reviewer’s report:

Minor Essential Revisions:

Although the authors showed clear results about its method for obtaining cancer stem cells from poorly differentiated or undifferentiated HCC cells, they must modify some parts of the manuscript, in order to clarify the results.

Some tables should be included, inside a figure or as a separated table. This is required for figures 4, 5 and (maybe) 7. These tables should be accompanied by the deletion of all percentages referring these figures included in the text. As an example: "CD24 positive: HLE, 88.1%; HLE-sphere, 58.6%; SK, 32.2%; SK-sphere, 11.4%; CD90 positive: HLE, 83.9%; HLE-sphere, 43.6%; SK, 75.7%; SK-sphere, 13.1%; Fig. 5". In a table, or a barchart, these percentages will be clearer to read.

In figure 1 and 2, they should use the same scale for all micrographs. In addition, the morphology of SK cells in micrograph of Figure 2F is not clear. I think that are "spheroids adherents", according to the text, but it should be clarified.

Level of interest: An article whose findings are important to those with closely related research interests

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