Reviewer's report

Title: Sphered cell subpopulations with cancer stem cell properties in human hepatoma cell lines

Version: 2 Date: 21 April 2011

Reviewer: Nicholas Barker

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Minor Essential Revisions:

1) The inclusion of data demonstrating resistance to a range of therapeutic agents certainly strengthens the manuscript. However, I still think important mechanistic insight would be provided by a simple analysis of candidate CSC marker expression in the spheres following treatment. Is there selection for CSC phenotypes within the spheres following treatment, as has been suggested as a contributing factor in tumor relapse in patients?

2) It is also surprising that no enrichment for CD133 was seen using IF in the spheres, despite this being evidenced by Western blot in figure 4B. Does this mean that CD133 isn't a good CSC marker? This should be discussed.

3) Please quantify the Western blots in Figure 5 - this is much easier for the reader to interpret.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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