

We wish to thank both reviewers for their time and effort in reviewing our manuscript. Both reviewers had only minor comments and suggested that we include a diagram to illustrate that the molecular pathways that regulate liver cancer stem cells (LCSCs). We have included such a figure to summarize the factors that regulate LCSCs. Reviewer 2 also suggested that we add additional sections to provide the background information. The following is our point-to-point response to the Reviewers' comments:

Reviewer 1

It is better for the authors to draw a frame diagram to show the relationship between stem cells and signaling pathways, epigenetic regulation, including DNA methylation, histone methylation and microRNAs.

A diagram illustrating the factors that regulate LCSCs has been added as suggested.

Reviewer 2

The manuscript outlines the key regulators of liver (sic) cancer stem cells. The content would be of interest for the investigators in the field. The authors are advised to add more sections with a bit of background and figures are essential for wider audience in related areas of research.

We thank the reviewer for indicating that our manuscript would be of interest to investigators in the field. As mentioned above in our response to Reviewer 1, we have now included a figure to illustrate the factors and pathways that regulate LCSCs. Regarding the background information, rather than adding more sections, which will disrupt the flow of the text, we expanded the Introduction section by adding more statements to discuss the characteristics and possible origins of cancer stem cells. We will be happy to add more background information, if Reviewer 2 feels that it is necessary and can provide more specific comments regarding what background information that we should include to further strengthen this manuscript. We thank the reviewer for the thoughtful comments.