Reviewer reports:

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: For rethinking the questions are below. 1. Does anchorage-independent cell culturing like in a low attachment plate or in polyhema, encourage condensation of BM-MSCs beside apoptosis during the experimental procedure? 2. Does anoikis may result in the death of all cells (un-inhibited Mst1) in a week as reflected in your results, due to the presence and improved ROS over time? 3. Does suspension cell culturing under high ROS presence under anoikis continue to grow or culture? The manuscript needs to add complete catalog numbers of all chemicals and kits that were used like autophagy inhibitor 3-MA?, array kits etc

To Reviewer 1:

Thank you for pointing this out.

Question 1. In the beginning of our experiment, we found that cell got condensation quickly. Thus, before cultured in Poly-HEMA coated well, we resuspended the cells into single. And after cultured in the well for 3 h, we resuspended the cells again.

Question 2. In our study, cells were not cultured for more than 48 h. Besides,

our study found that ROS level increased in detached condition. And previous study demonstrated that excessive ROS production led to anoiksi.

Question 3. In our study, we did not measure that whether cell culturing under high ROS presence under anoikis continue to grow or culture. We would like to address this problem in the future. We added catalog number, and highlighted these.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: The article arouses a lot of interest. First of all, congratulations to the authors of the study. It would be interesting to understand the timing of the analyzes and to make the cells expressing LC3 and p62 visible in immunofluorescence. Furthermore, it would be interesting to analyze the pathway of the genes involved in the induction of apoptosis and their related correlations.

To Reviewer 2:

Thank you for pointing this out.

1) It is difficult to observe the suspension cultured mBMSC expressing LC3 and p62 visible in immunofluorescence, thus, we analyzed the LC3

and p62 expression by Western Blot.

2) The genes involved in the induction of apoptosis and their related correlations will be explored in the next step in-depth study.

Reviewer #3:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: This study demonstrates that Mst1 plays a role in anoikis. In "Cell adhesion" section, please describe the calculation method of the cell viability more in detail.

To Reviewer 3:

Thank you for pointing this out. There is one slip of pen in this part. We rewrite this paper, and highlighted it.

After cultured in poly-HEMA-coated petri dishes, the collected cells were resuspended in the complete α-MEM medium and then plated in triplicates (5× 10^4 cells/well) onto the well coated with fibronectin (10 g/ml), which was previously blocked with 1% BSA for 1 h. After 6 h, the cells were washed with PBS and stained with crystal violet. Unbound dye was removed with PBS before using 10% acetic acid. The absorbance was read at 630 nm using a Multiskan MK3 microplate reader. The experiment was repeated thrice. Cell adhesion was calculated according to the the

proportion of the control group.

Journal editor-in-chief review respond report

I am pleased to receive your reply. Here is our reply.

Question 1, 2, 3, 4, 6, 10: I have corrected these mistake, and highlighted them in red.

Question 5: In this paper, we tested whether mBMSC/sh-Mst1 administration induced tumour‐like mass formation. And no between-group statistics were performed.

Question 7: In these references, they all showed that mesenchymal stem cells offer a therapeutic approach for pulmonary arterial hypertension related to their anti-inflammatory, immunomodulatory, regenerative properties. We cited these references for proving that Mst1 inhibition may improve these properties of MSCs.

Question 8: I did not understand this problem.

Question 9: I reuploaded the PPT contained Fig. 4.