

Peer Review File

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Reviewer Comments

Comment 1: It's excellent work, but some adjustments are needed. The authors don't show the expression profile of LRP6 in MCF7 or even after the inhibition by si-LRP6. These results are necessary to understand the expression profile in the parental cell and the efficiency of inhibition. I suggest that this result be displayed before the functional tests.

Reply 1: Thanks for your suggestion. We have added the relative expression levels of LRP6 in MCF-10A and MCF7 cell lines, as well as the relative expression of LRP6 in NC group and si-LRP6 knockdown group in Figure 3.(see page 27, Fig 3 A and B,line501)

Changes in the text: Page 27, Fig 3: we added Fig 3A and 3B. Page 28, line 501: we added the figure legends of Fig 3A and 3B.

Comment 2: Line 288: Knockout and knockdown are different processes. Check that and use the correct term.

Reply 2: Thanks for your suggestion. We have checked the text and changed "knockout" to "knockdown". The siRNA technique we used is to knockdown the expression of LRP6.(see Page3,line57;Page4,line70,line72;Page8,line167;Page15,line295,line300;Page18,line363)

Changes in the text: We changed "knockout" to "knockdown" (see Page3, line57;Page4,line70,line72;Page8,line167;Page15,line295,line300;Page18,line363)

Comment 3: Line 307: The authors discussed triple-negative breast cancer. However, the significant results are about luminal tumors and all experimental assays as well. I'd like to read something about luminal tumors here.

Reply 3: Thanks for your suggestion. Due to the important results about luminal subtype, we discussed the current treatment and problem topics of luminal subtype. We have modified our text as advised (see Page16, line319-324)

Changes in the text: Page16, line319-324

Comment 4: Line 312: The text fits better in the introduction. The authors do not mention the Wnt/B-catenin pathway in the introduction and could gain much by writing about it, as it locates the reader on the importance of LRP6.

Reply 4: Thanks for your suggestion. In my opinion, the discussion of Wnt/ β -catenin pathway is very important for the study of the importance of LRP6. Therefore, the adjustment of this part into the introduction can better arouse readers' thinking about the importance of LRP6. We have modified our text as advised (see Page5-6,line102-113)

Changes in the text: adjust the position of the second paragraph in the Discussion

part of original manuscript to Introduction(see Page5-6,line102-113)

Comment 5: Line 327: Correct "levles" to "levels"

Reply 5: Thanks for your suggestion. All mistakes in grammars have been corrected (see Page 16, line 329).

Changes in the text: Page 16, line 329: levels

Comment 6: Line 328: "... and breast cancer is". You can use ARE here, not IS.

Reply 6: Thanks for your suggestion. All mistakes in grammars have been corrected (see Page 16, line 331).

Changes in the text: Page 16, line 331; IS was modified as ARE

Comment 7: Line 361: See more about this term: "knocking out".

Reply 7: Thanks for your suggestion. All mistakes in grammars have been corrected. We have modified the text as advised.

Changes in the text: We changed "knockout" to "knockdown" (see Page3, line57; Page4, line70, line72; Page8, line167; Page15, line295, line300; Page18, line363)

Comment 8: Fig.2. It starts with the letter D. I suggest starting with the letter A because it is not a continuation of figure 1. You can use the acronym for "Overall Survival" as you determined before and the full term is not necessary all the moment.

Reply 8: Thanks for your suggestion. We have renumbered the Fig2 and use the the acronym for "Overall Survival". We have modified the text as advied(see Page24-26, Fig2ABCDE)

Changes in the text: see Page24-26, Fig2ABCDE

Comment 9: Line 504: Fig3. You can start with the letter A.

Reply 9: Thanks for your suggestion. We have renumbered the Fig3. (see Page 26-28, Fig3)

Changes in the text: Page 26-28, Fig3

Comment 10: Line 508: Fig4. You can start with the letter A.

Reply 10: Thanks for your suggestion. We have renumbered the Fig4 .(see Page 28 ,Fig4AB)

Changes in the text: Page 28, Fig4AB

Comment 11: I suggest you an English review.

Reply 11: Thanks for your suggestion. All mistakes in grammars have been corrected.

Changes in the text: We have modified the text as advied.