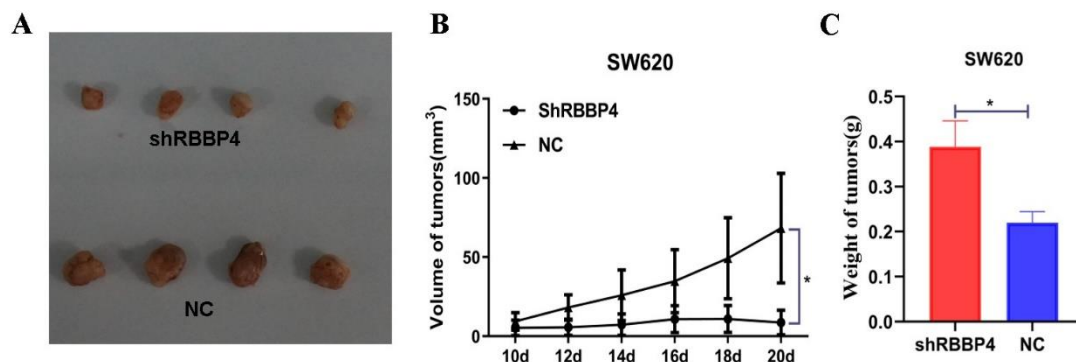


Dear Editors and Reviewers,

Thank you for your letter and for the reviewers comments concerning our manuscript entitled “RBBP4 promotes colon cancer malignant progression via regulating Wnt/ $\beta$ -catenin pathway” (ID:58059). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. Revised portion are marked in red in the paper. The main corrections in the paper and the responses to the reviewer's comments are as following:

**Comment 1: It is necessary for the authors to perform animal experiments.**

Reply: This is a valuable suggestion. According to this suggestion, we did the nude mice tumorigenicity experiment with SW620 cells transfected with RBBP4 shRNA or negative control. And as the same with the proliferation *in vitro*, RBBP4 knockdown showed significantly inhibition of tumor growth in nude mice. However, the further verification of the effect of RBBP4 on the Wnt/ $\beta$ -catenin pathway *in vivo* needs some time to complete. The primary results are shown below.

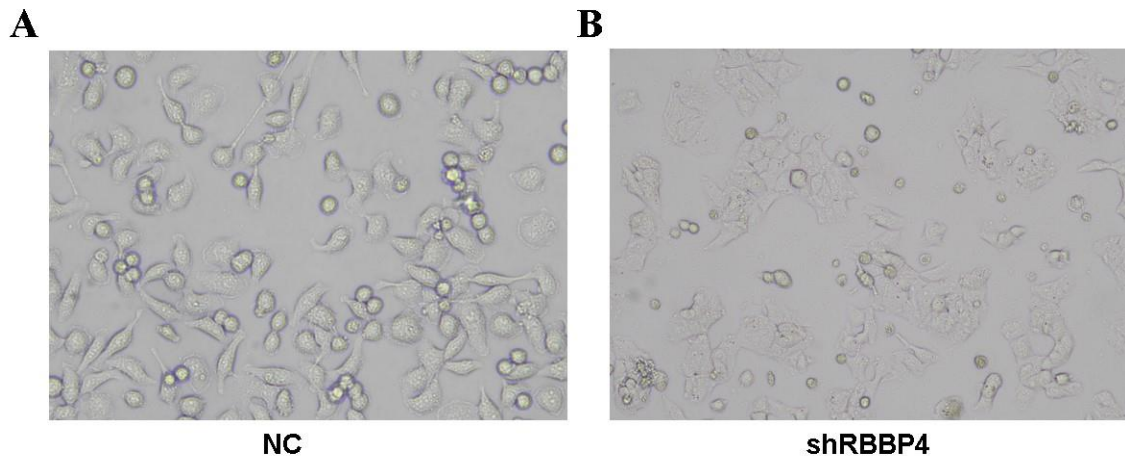


The effect of RBBP4 knockdown on the tumorigenicity *in vivo*. (A) The macroscopic picture of the tumors. (B) The growth curve of tumors. The subcutaneous tumor size was calculated and recorded every four days using the following equation: tumor volume = (length  $\times$  width<sup>2</sup>)/2. (C) The weight of

tumors.

**Comment 2: Authors performed the genetic manipulation on the cell lines, do the cell lines change the morphology to indicate EMT as claimed in the manuscript?**

Reply: Yes, we observed the morphology change during our experiments. As shown in the pictures below, the spindle shaped cells in SW620 cells with shRBBP4 was decreased, and cells tend to be round.



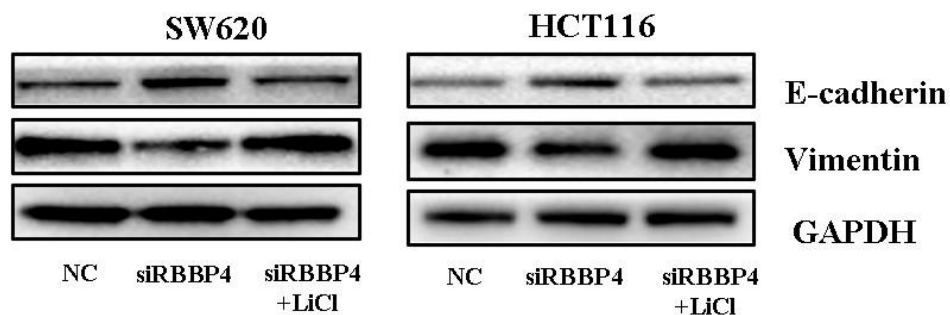
The cell morphology of Sw620 with RBBP4 knockdown (right panel) or NC (left panel).

**Comment 3: Figures 1 and S1 need to be integrated.**

Reply: We have integrated Figures 1 and S1. Figure S1 was changed to Figure 1G.

**Comment 4: In rescue experiment, the authors detect the viability and invasion of SW620 and HCT116 cells. It is necessary to exam EMT-related proteins and migration of SW620 and HCT116 cells.**

Reply: Thank you for this constructive suggestion. We examined the EMT-related proteins and the result was added as Figure 5E. For the cell invasion and migration were both examined by transwell assay, we just examined the cell invasion of SW620 and HCT116 cells.



The EMT-related proteins expression in the rescue experiment.

**Comment 5: In Fig 1.B, where are error bars?**

Reply: Thank you for your careful work. When we draw this figure, we just adopted the data from one experiment. And we have corrected this mistake and re-draw this figure.

**Comment 6: In the statistical analysis section, the authors mentioned that the statistical tests were performed by SPSS and Prism? Which one do the authors used? If it is SPSS, what type statistical tests were performed?**

Reply: We are sorry for the confused description. The histograms in the figures was drawn and analyzed by Graphpad Prism version 7.0, and the P value was verified by SPSS. Student's *t* test and one-way analysis of variance were conducted to analyze differences between groups. We corrected this in the manuscript.