Dear Editor:

Thank you very much for your letter and advice. We have revised the manuscript (Manuscript No.: 47761), and would like to re-submit it for your consideration. According to the Reviewer and Editors' recommendations, we have modified the manuscript. Point by point responses to the Editor and reviewer's comments are listed below.

Replies to Editor:

Answer: Thank you for your advice. We have now modified the manuscript according to the comments and included an audio core tip file, titled"47761-Audio CoreTip.mp3".

Replies to Reviewer:

Reviewer 1:

The novel findings of the manuscript concern the role of miR-205 and APC in pancreatic cancer, in that upregulation of this miRNA in cancer may promote tumorigenesis through downregulation of APC, as well as modulation of other signaling pathways. This can have therapeutic applications in the future. Problems: 1. Spelling and grammar errors - it needs to be edited. 2. the qRT-PCR - Is there any data that demonstrate whether the RNA used is DNA free? Trizol isolation is not necessarily going to get rid of all the DNA, and I do not see any indication that any subsequent DNase step was performed. Therefore, is there any negative control, such as doing the RT-PCR but skipping the RT step? If the RNA is really DNA free, then performing PCR directly on the RNA should not yield a band. Can the authors comment on this, at least? If they have any of these RNA samples left over, showing that no product is formed without the RT step would be helpful. Or do you use primers that span exon/intron junctions and thus can distinguish DNA from fully processed RNA? 3. You would expect that downregulation of APC would increase Wnt signaling. Although the authors did not directly assay for this, I did see some Wnt-related "hits" in Fig. 3. The authors should comment more about this in the Discussion. I did see one paper claiming PANC-1 cells have low levels of beta-catenin (some other form of control?).

Answer:

1. Spelling and grammar errors have been corrected in the revised version.
2. We have added information about qRT-PCR in Material and Methods section, "total RNAs were isolated from each sample by Trizol (Invitrogen, CA, USA) and treated with DNase I (Invitrogen, CA, USA) to remove residual DNA respectively".
3. We have discussed this issue in Discussion section "The target prediction of miR-205 and functional enrichment analysis of the targets identified genes were involved in various functions and pathways, including Cytokine–cytokine receptor interaction,

Regulation of IFNA signaling, Wnt-signaling pathway and TGF−beta signaling pathway. Among them, Wnt signaling pathway was demonstrated to regulate crucial aspects of cell fate determination, cell migration, and organogenesis. Previous study found that mutations cause Wnt pathway activation in human cancers".

Reviewer 2:

Depite the fair quality of the results, the overall level of writing is poor and the manuscript should be rewritten in order to be accepted for publication.

Answer: Thank you for your valuable suggestions, we have modified the language of the manuscript.

Reviewer 3:

Researchers aimed to reveal the relationship of miR-205 with pancreatic cancer. The analyzes conducted in this direction are sufficient and supportive analyzes for demonstrating this relationship.

Answer: We are pleased to note the favorable comments in the opening sentence and we would like to express our sincere appreciation for your careful reading and valuable comments.

We hope that the revised version of the manuscript is now acceptable for publication in the journal. If any question arises, please let us know.

Thank you very much for your consideration.
With best wishes.

Yours sincerely,
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