Dear editor,

Re: Resubmission of manuscript number 57286

On behalf of my co-authors, I would like to thank you for your prompt review of our manuscript titled, lncRNA C9orf139 can regulate the growth of pancreatic cancer by mediating the miR-663a/Sox12 axis.

In support of our resubmission, we have revised our manuscript and addressed the reviewers' comments in the following pages. All revisions to our manuscript have been highlighted using Track Changes in Microsoft Word.

We thank you in advance for reviewing our revised manuscript and our responses to the reviewers' comments. With these revisions, we hope that our manuscript is now acceptable for publication in the World Journal of Gastrointestinal Oncology.

Yours sincerely,

Min-Jie Wei

Reviewer # 1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language
polishing) Conclusion: Minor revision

Specific Comments to Authors: This manuscript is a nice and important basic study about the new potential treatment target in pancreatic cancer. The abstract, core tips, key words, materials and methods are adequate. The article contains 33 references. Table and pictures are also adequate. The authors found that lncRNA C9orf139 could promote the growth of pancreatic cancer by mediating the miR-663a/Sox12 axis, but the title of the manuscript is "LncRNA C9orf139 inhibits pancreatic cancer cell growth by modulating miR- 663a/SOX12 axis". There is a clear discordance between the results and the title, this may be a typewriting error; for this reason the title should be corrected. After this correction, manuscript worth publishing.

Response: Thank you very much for your praise for this manuscript. There was a typewriting error in the title, we have revised the title.

Reviewer #2:

Scientific Quality: Grade B (Very good)
Language Quality: Grade A (Priority publishing) Conclusion: Accept (General priority)

:specmc comments to Autnors: I read me article carretully I would like to accept tnis well written article

as it is. It adds novel information about pacreatic cancer genetics to the literature. Thank you.

Response: Thanks for your praise. We will work hard to perfect this study.

Reviewer #3:

Scientific Quality: Grade B (Very good)

Language Quality: Grade
B (Minor language
polishing) Conclusion:
Accept (General priority)

Specific Comments to Authors: It is a well written paper to evaluate the function of tumor suppressor lncRNA C9orf139 in pancreatic cancer progression and to study the underlying mechanism in a series of 54 patients. No comments.

Response: Thanks for your praise. We will work hard to perfect this study.

Reviewer #4:

Scientific Quality: Grade C (Good)

Language Quality: Grade
A (Priority publishing)
Conclusion: Minor
revision

Specific Comments to Authors: In this Study the Authors evaluate the function of tumor suppressor LncRNA C9orf139 in pancreatic cancer progression. The Abstract and Introduction sound well. I recommended adding the References in last part of Introduction: "Previous Studies have found that mi R-663a is lowly expressed in…" (References).In Materials and Methods the Authors must better exdplain how and how much tumor tissue was collected. The Authors have to explain if the 2 groups (cancer patients and control group) were homogeneous or not in gender and age. Statistical analysis and Results are good. Discussion is good.

The Authors must correct reference n. 20: the first name is wrong.

Response: Thanks for your comments. We have added a reference for this sentence "Previous Studies have found that mi R-663a is lowly expressed in…" in the INTRODUCTION part. We have also detailed the collection of tumor tissues and the difference in the baseline data between cancer patients and normal participants. Besides, we have corrected reference No. 20.

Reviewer #5:

Scientific Quality: Grade B (Very good)

Language Quality: Grade
B (Minor language
polishing) Conclusion:
Accept (General priority)

Specific Comments to Authors: This is a manuscript looking at lncRNA C9orf139 in relation to oncogenesis in PDAC. The first part looks at comparing expression levels in serum and tissue in 54 PDAC patients from 2013 to 2014 with a 5 year follow up, and compares this to expression in serum in 30 "normal" individuals. It is unclear how these "normal" patients were determined but appears to be "clinically" normal but without mention of imaging studies or other investigations to exclude pancreatic disorders including premalignant states. Figure 1A which shows levels in PDAC and controls seems to show some overlap between samples and it would actually be better if the comparison had also included serum and tissue from a cohort of patients who had surgery for non-malignant pancreatic disorders, e.g. cystic neoplasms. In Figure 1B, it shows "precancerous" tissue, but it is unclear what this means as in the methodology it is described as "adjacent" tissue. The definition of expression levels into high and low is not clearly stated and it is uncertain how this separation into 27 high and 27 low expression levels is done. The cell line and animal model studies that demonstrate knockouts of C9orf139 inhibiting growth of PDAC cells, and the inhibition of miR663a and mediation of SOX12 to increase PDAC cell growth are well demonstrated in Figures 2 to 5. The conclusions are reasonable. There is a need for minor language revision regarding terminology

and expression.

Response: Thanks for your comments. We have checked this manuscript thoroughly to address those problems according to your suggestions.

1. It is unclear how these "normal" patients were determined but appears to be "clinically" normal but without mention of imaging studies or other investigations to exclude pancreatic disorders including premalignant states.
   Response: All included normal participants were not affected by disease involving the pancreatic system. We have stated this in the inclusion and exclusion criteria
2. Figure 1A which shows levels in PDAC and controls seems to show some overlap between samples and it would actually be better if the comparison had also included serum and tissue from a cohort of patients who had surgery for non-malignant pancreatic disorders, e.g. cystic neoplasms.
   Response: This is a good suggestion. But we did not collect peripheral blood from patients with non-malignant pancreatic diseases (such as cystic neoplasms) in this study, so it is difficult to make such comparison and provide corresponding pictures. We will carry out follow-up trials according to your suggestion to supplement our conclusions.
3. In Figure 1B, it shows "precancerous" tissue, but it is unclear what this means as in the methodology it is described as "adjacent" tissue.
   Response: We collected tissues adjacent to lesions in this study. We have modified the figure.
4. The definition of expression levels into high and low is not clearly stated and it is uncertain how this separation into 27

high and 27 low expression levels is done.

5. **Response: The separation into high and low expression levels was based on the median expression value of C9orf139. We stated this in the RESUTLS section.**
6. There is a need for minor language revision regarding terminology and expression.

Response: The language in this manuscript has been improved by a native English speaker.