

Dear Editor,

We thank you for the positive comments regarding our manuscript entitled "*Circ\_0003356 suppresses gastric cancer growth through targeting the miR-668-3p/SOCS3 axis*". We have considered your comments and have made all the required revisions to the text and figures. We agree that the quality of the manuscript is now improved and hope that you now deem this accepted for publication.

**Reviewer #1:**

**Specific Comments to Authors:**

Li et.al found that circ\_0003356 expression was positively related to GC patient prognosis, which is down-regulated in GC tissues and cells. Then, they confirmed that circ\_0003356 up-regulation or miR-668-3p down-regulation could repress migration, viability, proliferation, EMT, and invasion of GC cells and facilitate GC cell apoptosis. In xenograft mice, circ\_0003356 up-regulation could suppress tumor growth. Meanwhile, they targeted miR-668-3p by circ\_0003356, and SOCS3 was targeted by miR-668-3p. Finally, they reversed EMT by miR-668-3p up-regulation or SOCS3 down-regulation in GC cells. These findings are very interesting.

**Minor comments:**

1. The exact p values should be provided in the main text across the manuscript.

**Response 1:** Thank you for your comment. We have added exact p values in the results section of the revised manuscript.

2. The references for published GEO database and GSE184882 dataset should be added.

**Response 2:** The references for the published GEO database and GSE184882 datasets have been added (references 25 and 26 in the revised

manuscript).

3. In Figure 4, the corresponding quantitative values for biology experiments should be described and analyzed in the main text.

**Response:** Thank for the comment. We agree and have added the corresponding quantitative values for all experiments in the results section of the revised manuscript.

**Reviewer #2:**

**Specific Comments to Authors:**

This study demonstrates that circ\_0003356 can inhibit the growth of gastric cancer.

- 1 The targeted sequences of miR-668-3p in SOCS3 may be explained in detail in "SOCS is targeted by miR-668-3p" in page 12.

**Response 1:** Thank you for the comment and this has been revised. The targets were searched using the starbase2.0 database. We identified SOCS3 binding sequences (AGUGAC) of miR-668-3p (shown in Figure 5A). Relative luciferase activity in AGS ( $0.37 \pm 0.06532$ ) and HGC-27 cells ( $0.32 \pm 0.06532$ ) transfected with SOCS3 WT reporter was evidently reduced in response to transfection of miR-668-3p mimic ( $P = 0.00041$ ,  $P = 0.00065$ ,  $P < 0.001$ ; Figure 5B). The SOCS3 MUT reporter showed no such changes after miR-668-3p mimic addition (Figure 5B), suggestive of a direct interaction between miR-668-3p and SOCS3. These descriptions have been included in the revised manuscript.

2. Pictures in Figure 6 may be more clearly shown.

**Response 2:** Thank you for the comment. We have revised Figure 6 to ensure clarity across the images. At the same time, we have revised Figure 3 and Figure 4 due to some problems.

## **EDITORIAL OFFICE'S COMMENTS**

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) Science editor:

The manuscript has been peer-reviewed, and it's ready for the first decision.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade C (Good)

**Response:** Thank you for the positive comments.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report and the full text of the manuscript, all of which have met the basic publishing requirements of the World Journal of Gastrointestinal Oncology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

The quality of the English language of the manuscript does not meet the requirements of the journal. Before final acceptance, the author(s) must provide the English Language Certificate issued by a professional English language editing company. Please visit the following website for the professional English language editing companies we recommend:

<https://www.wjgnet.com/bpg/gerinfo/240>.

**Response:** Thank you for the comment. We have sought a professional English language editing company who have proofread and modified the article. We

have provided the English Language Certificate as a supplementary file.

Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the Reference Citation Analysis (RCA). RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>.

**Response:** To improve the content of the manuscript, we have edited the highlights section to fully showcase the impact of our findings.

Uniform presentation should be used for figures showing the same or similar contents; for example, "Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...".

**Response:** Thank you for the comment. We have revised the figure legends according to above requirements.

Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2022.

**Response:** We have provided decomposable Figures as a PPT file. Moreover, our figures are original, and we have added the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT):  
Copyright ©The Author(s) 2022.

With regards,

Yao Wang