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Dr. Li Ma
Science Editor, Editorial Office Director, Company Editor-in-Chief, Editorial Office
World Journal of Gastrointestinal Oncology
Baishideng Publishing Group Inc.
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: l.ma@wjgnet.com

RE: Resubmission of our manuscript (ID #84819, Basic Study)

Dear Dr. Ma:

Thank you very much for your email with encouraging news regarding our manuscript. We also thank the reviewers for their positive/constructive comments and suggestions, which helped us improve our manuscript. After incorporating their comments into the revised manuscript, I would like to re-submit it for your consideration for publishing in the *World Journal of Gastrointestinal Oncology*. The amendments are highlighted in red in the revised manuscript. Our point-by-point answers to the reviewers' comments are attached below. This revised manuscript has been edited and proofread by *Medjaden* Bioscience Limited (Wuhan, China).

Thank you again for your valuable input. I hope that the revision is acceptable. I am looking forward to hearing from you soon.

Sincerely,

Li Xiang, PhD
Department of Gastroenterology
The Second Affiliated Hospital of Chinese University of Hong Kong
Shenzhen Longgang District People's Hospital
Shenzhen, Guangdong 518172,
China
Email: shellyxiangli@163.com

Our responses to the reviewers' comments:

Reviewer #1:

1.
Some English editing is required. The use of long sentences should be avoided. For instance, the sentence in the Abstract (Lines 55-56: “This study investigated miR-188-
3p expression and its roles and underlying molecular events in gastric cancer”) – can be impr oved and made easier for understanding. It should be (a suggestion): This study investigated miR-188-
3p expression and its role in the regulation of gastric cancer (GC) growth. The underlying mo lecular events were targeted.
We thank the reviewer for the valuable advice. We have revised our manuscript accordingly. This revised manuscript has been edited and proofread by *Medjaden Inc.*

2.
I recommend to avoid using phrases like “Towards this end,..” line 98. Authors should use co ncise academic language.
Indeed, we followed the reviewer’s suggestions during the revision of our manuscript accordingly, and this revised manuscript has been edited and proofread by *Medjaden Inc.*

3. Introduction may need to accent the role of epigenetic regulation as a promising therapeuti c target in cancers. For instance, authors may check this review https://pubmed.ncbi.nlm.nih. gov/35623562/
We thank the reviewer for the advice. We read and cited it in the revised manuscript (Page 5, Line 121-124).

4. Line 149 onwards: authors should cite relevant papers which used those cell lines, indicate d in this section. Some cells lines are not well known. For instance, I could not find any refer ences for BGCBGC-823. Overall, the methods section needs more citations.
We thank the reviewer for the advice. We have fixed the typo accordingly. We also added cited refs (*Zhuo W, Liu Y, Li S, Guo D, Sun Q, Jin J, Rao X, Li M, Sun M, Jiang M, Xu Y, Teng L, Jin Y, Si J, Liu W, Kang Y, Zhou T. Long Noncoding RNA GMAN, Up-regulated in Gastric Cancer Tissues, Is Associated With Metastasis in Patients and Promotes Translation of Ephrin A1 by Competitively Binding GMAN-AS. Gastroenterology. 2019 Feb;156(3):676-691.*
Xia X, Zhang G, Wang T, Ji M. The role and mechanisms of long non-coding RNA LINC00662 in promoting the proliferation, migration, and angiogenesis of BGC-823 and HGC-27 cells and the subsequent effect on the progression of gastric cancer. J Physiol Pharmacol. 2022 Dec;73(6).

5. Lines 240-
244: authors should indicate catalogue numbers for all used antibodies. including GAPDH, β-actin, CBL , LC3, Beclin 1, mTOR, p-mTOR, Akt (C-terminal), and p-
Akt (Ser473). The Cat# are essential information when others will try to repeat those experim ents.
The anti-GAPDH, β-actin, and CBL antibodies were obtained from Santa Cruz Biotechnology (Santa Cruz, CA, USA), anti-LC3 and Beclin1 were acquired from Cell Signaling Technology (Danvers, MA, USA), and a rabbit antibody anti-mTOR, p-mTOR,

Akt (C-terminal), and p-Akt (Ser473) antibodies were obtained from Cell Signaling Technology). We accordingly added the information in the revised manuscript (Page 8, Line 246-251).

6. Immunohistochemistry (IHC) figures (Fig.2,4, and 6) are too small and hard to evaluate. A uthor should present all IHC tissue images separately using larger magnification. IHC provid e the essential information about cancer cells and should be clearly presented.
We added high-resolution IHC images (Fig. 4 and 6) in Supplementary Figures 2A and 3 per the reviewer's advice.

7. Fig.2 A is very dark. It should be presented as a large version with a better quality. The aut hors tried to present more information, more data in one figure. This resulted in poorer qualit y of the presentation. Authors may need to extend the number of figures and present some dat a as Supplementary figures. However, the quality of images should be improved (images sho uld be enlarged, magnification should be increased). Otherwise, the images are useless.
We added high-resolution images (Fig. 2EFG) in Supplementary Figure 1 per the reviewer's advice accordingly.

8. Discussion: the controversial role of autophagy should be discussed. Authors should indic ate that autophagy may be activated during development of cancer resistance. Therefore, the complexity of autophagic pathway should be indicated.
We revised some discussion sections accordingly (Page 14, Line 433-440).

Reviewer #2:
The aim of this study was to investigate the expression and clinical significance of miR-188-3p and CBL in 50 gastric cancer and paired normal tissues. The research verified the antitumor activity of miR-188-3p in gastric cancer. The data is preliminary in vitro, and it is needed to get more research in the role of miR-188-3p in cancer.

We fully agree with the reviewer's opinion. Our *in vitro* experiments are indeed preliminary, and more in-depth investigation is needed in our future research venture.

Reviewer #3:
The authors presented an interesting manuscript. It is written on the basis of experimental studies and received clinical material of gastric cancer. The authors studied in their research the effect of antitumor activity of miR-188-3p in gastric cancer carcinogenesis. The molecular genetic impact of microRNAs has been proven for apoptosis, autophagy, and the process of cancer cell metastasis. The results of the study were confirmed on mice of a pure line. This research scientific is of great practical importance for clinical oncology. The results need to be used for the diagnosis of early gastric cancer and targeted therapy of this neoplasm. This scientific topic needs to be continued. The manuscript is recommended for publication.
We thank the reviewer for the excellent summary of our work, the positive remarks, and the constructive suggestions. We revised our manuscript according to the journal styles and all reviewers' suggestions.