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Reviewer A

1: The authors only used several cell lines. More human GC cell lines (NCI-N87, MKN74, NUGC-3, MKN45, MGC803, and HGC-27) were needed to verify the results. Additionally, was EDIL3 expression level negatively correlated with the differentiation status of the cells?

Response 1: Thanks for your suggestion, we have added human GC cell line MKN45 to verify the results in Figure 1-7. The corresponding methods, descriptions and figure legends were modified in the revised manuscript. In addition, EDIL3 expression level is positively correlated with the differentiation status of the cells.

Changes in the text: We have added MKN45 cells to verify the results in Figure 1-7. And the corresponding methods, descriptions and figure legends were modified in the revised manuscript.

2: Expression of EDIL3 in GC tissues of patients and their corresponding noncancerous mucosal tissues should be analyzed by IHC or WB.

Response 2: Thanks for your suggestion, we have added the expression level of EDIL3 in GC tissues of patients and their corresponding noncancerous mucosal tissues in Figure 1A by WB.

Changes in the text: We have added the expression level of EDIL3 in GC tissues of patients and their corresponding noncancerous mucosal tissues in Figure 1 by WB. And the corresponding methods, descriptions and figure legends were modified in the revised manuscript.

3. Kaplan–Meier survival analysis of GC patients with high or low EDIL3 should be supplied.

Response 3: Thanks for your advice. We have added qPCR results to determine the mRNA expression level of EDIL3 in GC tissues of patients and performed survival analysis in Figure 1B.

Changes in the text: We have added survival analysis of EDIL3 expression in Figure 1. And the corresponding methods, descriptions and figure legends were modified in the

revised manuscript.

4. Tumorigenesis experiment should be made in nude mice.

Response 4: Thank you for your advice. Following your suggestion, we have added tumorigenesis experiment in nude mice to determine the effect of EDIL3 on the development of gastric cancer.

Changes in the text: We have added tumorigenesis experiment *in vivo* to determine the effect of EDIL3 on the development of gastric cancer in Figure 7. And the corresponding methods, descriptions and figure legends were modified in the revised manuscript.

5. The relative protein levels of EDIL3 and XIST in gastric cancer cells should be confirmed by western blot

Response 5: Thanks for your suggestion, we have added the expression level of EDIL3 in Figure 1-5 by WB. And the corresponding methods, descriptions and figure legends were modified in the revised manuscript.

XIST is a long non-coding RNA X-inactive specific transcript RNA (lncRNA XIST), which cannot be detected by WB.

Changes in the text: We have modified the method, description and figure legends of corresponding WB in Figure 1-5 in the manuscript.

6. What is the Clinicopathological characteristics of patients with HCC according to EDIL3 expression.

Response 6: EDIL3 is elevated in HCC. High level of EDIL3 protein is much more commonly in patients with larger tumor or portal vein tumor thrombus formation, associated with poor prognosis. (Mol Cancer. 2014;226. pii:1476-4598-13-226. doi:10.1186/1476-4598-13-226.)

7. cell cycle experiments should be added.

Response 7: Thanks for your advice, we have added cell cycle experiments in Figure 1-5. And the corresponding methods, descriptions and figure legends were modified in the revised manuscript.

Changes in the text: We have modified the corresponding methods, descriptions and figure legends for the cell cycle experiments in Figure 1-5 in the manuscript.

8. EDIL3 overexpression experiment is needed.

Response 8: EDIL3 is highly expressed in gastric cancer tissues and cell lines, so we knocked down EDIL3 to verify its effect on GC. Furthermore, our primary goal is to explore the molecular mechanism of EDIL3 in the regulation of gastric cancer, but not its role.

Reviewer B

This paper can be strengthened by the following revisions:

1. The role each component the EDIL3/TGF-β1/XIST/miR-137 feedback loop is well studied. However, the upstream and downstream relationship of the four components is relatively weak. To solve this problem, several rescue assays should be performed. Firstly, to comfirm that TGF-β1/XIST/miR-137 are the downstream effectors of EDIL3, it is better to investigate whether recombinant TGF-β1 treatment, XIST overexpression can rescue the inhibitory role of EDIL3 knockdown on cell proliferation, migration, invasion and EMT in AGCs cells. Secondly, to confirm EDIL3 is the downstream of miR-137, besides the analysis of the 3'-UTR and dual luciferase reproter assay, it will be more convincing if EDIL3 overexpression resuces miR-137 mimics downregulated cell proliferation, migration, invasion and EMT in AGCs cells.

Response 1: Thanks for your suggestion, we had added recovery experiment in Figure 6 to verify that TGF-β1/XIST/miR-137 are the downstream effectors of EDIL3, and EDIL3 is the downstream of miR-137, respectively.

Changes in the text: The corresponding methods, descriptions and figure legends of Figure 6 were modified in the revised manuscript.

2. The study will be more significant if the author can detect the expression of EDIL3 in GC patient tissues and the corresponding non-tumor tissues, and even analyze the correlation between EDIL3 expression and the clinicopathological characteristics of GC patients.

   Response 2: Thanks for your advice. We added the expression level of EDIL3 in GC patient tissues and the corresponding non-tumor tissues in Figure 1A by WB. And we also added correlation analysis between EDIL3 expression and

clinicopathological characteristics of GC patients in Table1.

Changes in the text: Correlation analysis of corresponding detection and clinicopathological features were added in Figure 1A and Table1, and the description and figure legends were modified in revised manuscript.

3. In Figure 1, only RT-qPCR is not enough to verify the transfection efficiency of shEDIL3, Western blot should performed to confirm this result at protein level, which is more important.

Response 3: Thank you for your suggestion. We have added the knockdown efficiency detection of EDIL3 in Figure 1D by WB.

Changes in the text: And the corresponding methods, descriptions and figure legends of Figure 1 were modified in the revised manuscript.