*Cell Death & Disease* October 9th, 2018

Dear Professor ,

We appreciate for your letter about the information of our manuscript entitled “Epigenetic silencing of ZNF132 mediated by methylation sensitive Sp1-binding promotes cancer progression in esophageal squamous cell carcinoma (ESCC)”. The revised manuscript has benefited greatly from consideration and incorporation of the constructive and insightful comments from you and the reviewers. As for the reviewers’ comments, a point-by-point description of our responses is as follows, where the reviewers’ comments are in italics and our responses in Times New Roman type.

Enclosed is the revised version of the article with the title “Epigenetic silencing of ZNF132 mediated by methylation sensitive Sp1-binding promotes cancer progression in esophageal squamous cell carcinoma (ESCC)”.

Thank you so much for handling with our manuscript!

Sincerely,

Minghua Wang, Ph.D.

Professor,

Department of Biochemistry and Molecular Biology

Soochow University

**Reviewers’ Comments:**

**Referee #1**

1, Is there any difference in the methylation level of *ZNF132* in ESCC cell lines with different invasive and metastatic abilities?

We thanks this great question. *ZNF132* promoter methylation

2, Fig4 suggests that overexpression of ZNF132 could inhibit tumor growth. How about using demethylation drugs in treating ESCC?

**Reviewers’ Comments:**

**Referee #1**

**Referee #2**

Minor concerns:

1. Forced expression of ZNF132 in each assays including transwell and xenograft mouse model should be validated by western blot instead of real-time PCR.

Thanks for the reviewer’s suggestion. We have verified the expression of ZNF132 in a xenograft mouse model by western blot as suggested. The result is added in Figure 4F.

2. It will be nice to examine the protein expression pattern of ZNF132 in clinical ESCC samples besides the real-time PCR examination.

Thanks for the reviewer’s suggestion. I am very sorry that the amount of each clinical sample collected at that time was relatively small, and all were used to extract DNA and RNA for correlation analysis.

3. The scientific logic or references for analyzing Sp1 binding ability should be described in detail in P.13 after “As CpG was in silico predicted to be harbored in transcriptional activator Sp1-binding site at ZNF132 promoter……”

4. How the promoter region of ZNF132 in ESCC is hypermethylated should be further discussed.

The manuscript has been resubmitted to your journal. We look forward to your positive response.  
Thank you very much.  
Please contact me by E-mail: mhwang@suda.edu.cn, if there is any question.  
Yours sincerely,

Minghua wang