

Cover Letter

Dear Editor in Chief,

Thank you very much for offering us the opportunity to revise our manuscript entitled "Manganese superoxide dismutase (MnSOD) induction by AMPK activation protects hepatitis B virus expressing hepatoma cell line against apoptosis" (manuscript NO: 23628). We are grateful for constructive advice provided by you and the reviewer. We have revised the manuscript carefully according to the reviewer's comments and prepared the manuscript as your comment. And our manuscript has been reviewed for grammatical clarity and appropriate vocabulary by a colleague who has been doing research in the United States for many years and is good at English. Revised portions are highlighted in red text. Answers to the comments are attached below.

Thank you for your consideration, and we look forward to your reply.

Sincerely yours,

Yachao Yao, Ph.D

Department of Clinical Laboratory Medicine,
the Second People's Hospital of Guangdong Province,
Guangzhou 510317, China.

Phone: +86 020 89168136

E-mail: yaoyachaoll@163.com

Review 1

1. Generally, their findings seem to be interesting, anyway it should be validated in different cell lines, such as HepG2.117.

Answer: Thank you very much for the constructive suggestion. It is of great help if we could validate our findings with the cell line HepG2.117. Actually, we have been aware of this issue during our research. But unfortunately, there is no another available HBV-integrated HepG2 cell line for sale, and we also failed to get the cell line from other researchers. Therefore, we are afraid that we are unable to make experiments with HepG2.217 cell line at the moment. However, HepG2.215, as a typically representative HBV-integrated HepG2 cell line, is a commonly used cell model for the investigation of HBV-associated liver damage [Li W, Jiang Y, Wang X, et al. *PLoS One*. 2015, 10(8): e135874; Chen X, Wang Y, Tao J, et al. *Gastroenterology*. 2015, 149(3): 741-752; Liu D, Ni B, Wang L, et al. *FEBS Lett*. 2013, 587(20): 3314-3320.]. Moreover, our conclusion is supported by the results through several kinds of experimental methods and designs. Thus, we believe that our conclusion is convinced. We will, however, test other cell lines in our further studies.

2. Abstract: Please, remodel the aim.

Answer: According to the reviewers' suggestion, the aim was remodeled (See *Abstract*).

3. Material and methods: In the cell viability assay, authors do not show cell viability of knockdown HepG2.215 cells.

Answer: We had examined the cell viability of HepG2.215 cells after MnSOD knockdown. The result had been provided in Figure 3C.

4. Figures: Please, reconsider to include absorbance comparative data on figures 1A and 1B. It is also difficult to see Figure 1B, please check image quality.

Answer: We showed the result of cell viability in the same way as previous studies did [Li L, Yao Y C, Fang S H, et al. *J Biol Chem*. 2014, 289(44): 30785-30799.; Li J, Yao K, Yu X, et al. *J Biol Chem*. 2013, 288(50): 35671-35682]. So, we are not really sure what it means to include absorbance comparative data on figures. Additionally, the figure 1B was magnified partially for easily observation (See figure 1B).