Revision Letter

Dear Editor,

We were pleased to have an opportunity to revise our manuscript now entitled "NOX4 promotes tumor progression through the MAPK-MEK1/2-ERK1/2 axis in colorectal cancer (No.: 90598)". According to the reviewers' comments and suggestions, we have made changes in a point-by-point fashion. These changes were highlighted in our revised manuscript in yellow. The responses to the concerns raised by reviewers are below and are color coded as follows: a) Comments from editors or reviewers are shown as *text*; b) Our responses are shown as text.

The reviewers' comments were very helpful overall, and we are appreciative of such constructive feedback on our original submission. After addressing the issues raised, we feel the quality of the paper is much improved.

Yours sincerely,

Vista

Yi Zhang, MD, PhD Director, Biotherapy Center Co-Director, the Division of Research Distinguished Professor, Cancer Center The First Affiliated Hospital of Zhengzhou University Zhengzhou, Henan, 450052 P.R. China Tel: +86-371-66295320; +86-15138928971 E-mail: yizhang@zzu.edu.cn *Reviewer* #1: Authors posted their conclusions in the end of discussion section - it's better to post it in the separate conclusion section

A: Thank you for your comments. According to the reviewers' comments and suggestions, we have post our conclusions in the separate conclusion section instead of the end of discussion section