Author’s response to reviews

Title: Inhibiting MAPK14 showed anti-prolactinoma effect

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We are grateful to the reviewers for their valuable time and useful contributions to our manuscript. Here are our responses one by one.

Reviewer 1

1. In discussion, the authors should describe whether MAPK14 directly affect prolactin secretion and tumor growth. What is downstream pathway of MAPK14, any relationship with known mechanism of prolactinoma? Did MAPK knockout or suppression affect expressions of other p38 MAPK related proteins including MAPK 11-13?

The discussion has been significantly revised. Inhibition of MAPK14 reduced the secretion of PRL and growth of tumor (Discussion section, line 372, page 17). The downstream pathway of MAPK14 remains to be further studied and is completely different from the known mechanism of prolactinoma (Discussion section, line 373, page 17). This study only investigated the effect of knockout or inhibition of MAPK14 on prolactin adenomas. We are very sorry that due to the limited time, the role of other P38 MAPK related proteins including MAPK11-13 in prolactinoma is being studied.

2. It is better to describe what comprised of the "other pituitary disease". If it contains pituitary adenomas, show prolactin positiveness in pathology.

The "other pituitary disease" have been added (Background section, line 54, page 3). We are sorry that the pathology investigate was not conducted in this study.
3. Why don't you add clinical data of prolactinoma patients and investigate the relationship between serum prolactin values and MAPK14 expression or drug-resistance and MAPK14 expression? Because the Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology only provided paraffin samples for pituitary tumors, and no serum was collected from patients.

4. In statistics, the authors should state which post-hoc analysis after one-way ANOVA they used to compare the difference between groups. We are very sorry for the previous negligence, which has been added. Comparisons between difference groups were performed using a one-way ANOVA followed by a post hoc Tukey’s test (Methods section, line 249, page 12).

5. How human pituitary tumors were preserved, in formalin solution or in liquid nitrogen? Paraffin specimens of human pituitary tumors collected directly from hospital (Methods section, line 112, page 6).

6. It is better to describe how the authors analyze the immunofluorescent images, and show the name of the software they used. We are very sorry for the previous negligence, which has been added. The immunofluorescent images were analyzed using image-Pro Plus 6.0 software after microphotography (Methods section, line 163, page 8).

7. It is better to show immunofluorescent images of the pituitary gland of ES/MAPK14/-/- mice. We are very sorry that I didn't do this research.

8. It is better to state the name of the microscope and company. We are very sorry for the previous negligence, which has been added (Methods section, line 162, page 8).

9. Were mice in control group injected vehicle instead of ES? The control group did not receive an injection.

10. How the authors extract proteins from GH3 cells? We are very sorry for the previous negligence, which has been added (Methods section, line 224, page 11).

11. How long GH3 cells were treated with siRNA? 48h. We are very sorry for the previous negligence, which has been added (Methods section, line 217, page 10).

Reviewer 2
The English language has been revisioned.

We look forward to hearing from you regarding our submission. We would be glad to respond to any further questions and comments that you may have.