Author’s response to reviews

Title: Identification of novel candidate indicators for assessing zinc status during pregnancy in mice from microarray data

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Author’s response to reviews:

Dear editors and reviewers,

Thanks for your letter and the comments for our manuscript entitled “Identification of novel candidate indicators for assessing zinc status during pregnancy in mice from microarray data”. Those comments are all valuable and helpful for improving our paper, as well as the important guiding significance to our researches. Our manuscript has been checked and revised carefully according to reviewers’ comments and suggestions. The point-by-point responses to the reviewers’ comments were listed as below. We would like to re-submit this revised manuscript to “BMC Pharmacology and Toxicology” and hope it is acceptable for publication in the journal. Please do not hesitate to contact us with additional questions or concerns.

Reviewer reports:

Marina Galvez-Peralta, PharmD, PhD, FCP (Reviewer 1): Authors made a great effort to address all the asked questions/items.

My only two concerns are the different statements written without literature support (like the one related to consumption of zinc-rich food rather than medicines or the differences on placenta), and the lack of more extensive explanation of role of ZIPs/ZnT during embryogenesis and lack of Zn. (not only death, but other developmental problems).

Response: Thanks for your valuable comments. In this study, to make our statement more clear, we have revised our speculation that the best option is to consume dietary zinc (abundant in meat and beans) for improving mild zinc deficiency, rather than using medicines”, and we added the
references to support the statement, as follows: Notably, there is no currently available information that supports the routine use of zinc supplementation on improving pregnancy outcome [43]. Moreover, it is challenging to the implementation of targeted interventions for reducing the adverse effects of zinc deficiency through therapeutic and preventive supplementation, fortification, and biofortification [39]. Given the side effects of many drugs, especially to the fetus, the best option is to consume dietary zinc (abundant in meat and beans) for improving mild zinc deficiency, rather than using medicines.

Furthermore, we added more extensive explanation of the role of ZIPs/ZnT during embryogenesis and lack of Zn, as follows: Zinc is reported to exert antioxidant activity through guarding sulfhydryl groups and stabilization of cell membranes, and it may play a key role in modulating cell cycle and apoptosis [34, 35]. Two zinc transporter families, ZnTs and Zrt-, Irt-related proteins (ZIP) are shown to function in zinc mobilization across biological membranes [14]. For instance, ZnT 1 is shown to play a key role in zinc homeostasis in adult mice via modulating the transport of maternal zinc into the embryonic environment, and deletion of the Zinc Transporter 1 gene in mice may result in embryonic lethal [36]. ZIP8 could function indispensable effects on both multiple-organ organogenesis and hematopoiesis during early embryogenesis in mice [37]. Moreover, Zinc deficiency during pregnancy is harmful for both the mother and the fetus [38], which is considered as a risk factor for adverse pregnancy outcomes and preterm delivery [39]. As such, effective monitoring for zinc deficiency is very important.

We hope that the revised manuscript will meet with approval. Thank you very much again.

Beibei Huang, Ph.D. (Reviewer 2): Thank the authors for the responses to my questions, and the revision in the updated manuscript answered my questions.

Response: Thanks for your recognition of our work.

We appreciate for your warm work earnestly, and hope that the revised manuscript will meet with approval. Thank you very much again.

With kindest regards to you.

Yours sincerely,

Lixin Shang