

April 17th, 2016

Dear Editors of *World Journal of Methodology*,

Thank you for your encouraging decision letter about our submitted manuscript entitled “A Rat Model of Cholelithiasis with Human Gallstones Implanted in Cholestasis-Induced Virtual Gallbladder” (manuscript NO: 25783).

The comments from the reviewer have been carefully addressed point-by-point both in the manuscript (yellow highlighted) and in this revision letter (see attached page).

We hope that this revised version should meet the requirements for being published in *World Journal of Methodology* and eventually contribute to the ever-enhancing impact of your journal.

Sincerely yours

With my best regards,

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Responses to the Editors' Instructions

AE1: We would like to express our gratitudes to you and the 2 reviewers for your overall positive evaluation and your guidance in the revision of our article. Below, we seriously respond to the reviewers' comments and detail the corresponding changes.

Responses to the Reviewers' Comments

Reviewer 1 code 02445785 (R1):

Grade B (Very good); Grade A: priority publishing; Conclusion: Accept

R1A1: We are grateful for your appreciation of our work and your decision of acceptance of our manuscript to be published with your journal. Our manuscript has been further improved.

Reviewer 2 code 00694174 (R2):

R2Q: After having carefully reviewed this manuscript (ESPS Manuscript NO: 25783), which is quite interesting, I would like to recommend its publication in the World Journal of Methodology with the following comments. 1. This is an original research paper describing the methodology for establishing and validating a rat model of cholelithiasis, which therefore falls well into the scope of this journal. 2. I have searched from the internet and found that no similar model has been reported in the literature, i.e. an evident novelty. 3. In my opinion, creating a model of cholelithiasis in an animal species (such as the rat) that is even void of the visceral organ of gallbladder is very difficult and highly innovative. 4. Despite the technical challenges, the authors reported a high success rate of modeling, as supported by their convincing imaging, biochemical and histomorphological data. 5. A one-fit-all model hardly exists in reality, which also applies to the rat model of cholelithiasis described in this manuscript as the authors clearly recognized in the text. Although the model cannot be used to study the causes and influential factors in the formation of gallstones, it could be used to explore potential effects of therapeutic and diagnostic compounds for the management of cholelithiasis in human objects. 6. The manuscript is well written and organized. 7. I am curious about their new paper cited as Ref 17, in which this cholelithiatic model seems to be applied for a translational research, as the authors claimed.

R2A: First of all, we really appreciate Reviewer 2 for spending time to carefully go through our submitted materials, based on which the merits of our work were summarized. However, we do realize that everything is two-sided and have addressed its limitations in Discussion.