Author's response to reviews

Title: Effect of atorvastatin on the expression of gamma-glutamyl transferase in aortic atherosclerotic plaques of apolipoprotein E-knockout mice

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Author's response to reviews: see over
Dear Dr. Helmut Sinzinger:

Thank you very much for your letter and advice. We have revised the paper, and would like to re-submit it for your consideration. We have addressed the comments raised by the reviewers. This manuscript has been edited and proofread by International Science Editing, Compuscript Limited.

We hope that the revision is acceptable, and we look forward to hearing from you soon.

Sincerely,

Dr. Gang Li
**Reviewer:** Johann Auer

Did the authors measure modification of the oxidation state by additional biomarkers (like carbonyl groups, lipid peroxides and total antioxidant capacity)?

Due to the limitation of experiment conditions and funding, we failed to detect other biomarkers of oxidation state. This is a disadvantage of the present study. In our study, we used hs-CRP and IL-6 as a marker of systemic inflammation.

The authors state that “expressions of GGT-1, ICAM-1 and VCAM-1 in aorta were measured by RT-PCR”. Did the authors measure such expressions in the aorta or in the plaques. If the whole aortic tissue was measured, this should be clearly stated.

Thank you for your careful and patient review of our manuscript. We measured the whole aortic tissue and clarified it in the manuscript.

Did the authors perform a sample size calculation?

The sample size was calculated by $t$ test.

The dose of 5mg per kg seems to be very high. That may correspond to a daily dose of about 350mg atorvastatin in an adult subject (on average). Did the authors study dose dependent effects?

According body surface area (BSA) normalization method, we converted the drug dose between mouse and human. The dose of 5mg per kg was equivalent a daily dose of about 25mg atorvastatin in an adult subject. This was a normal dose for patients. So we did not take into account dose dependent effects. (Reagan-Shaw S, Nihal M, and Ahmad N. Dose translation from animal to human studies revisited. FASEB J. 2007; 22:659–661)

Minor comments:

The paper has to be revised with respect to grammar and style thoroughly.

This revised version was edited and proofread by International Science Editing Compuscript Limited.
Reviewer: Hazem F Elewa

Methods:

1- A clarification of the atorvastatin dose chosen is necessary. What is the equivalent of such dose in humans is important to clarify as well.

According body surface area (BSA) normalization method, we converted the drug dose between mouse and human. The dose of 5mg per kg was equivalent a daily dose of about 25mg atorvastatin in an adult subject. Your advice has been inserted in text (page 4, 2nd paragraphs, line 20-22).

2- Why was APOE KO mice used (rational for using such model)


Results:

2nd paragraphs, line 21: The interpretation of this correlation is not accurate. An r of 0.2 or 0.3 cannot be interpreted into strong correlation. It is actually a weak correlation.

According your advices, we have been corrected the strong correlation to weak correlation.

Discussion:

3rd paragraph, Line 5-7: The assumption made that the atorvastatin in this study made the plaque more stable and delayed its progression is not valid since there were no functional studies done in this research. Please make necessary changes.

Thanks for the reviewer’s advice. The assumption was deleted in the revised version.

Minor compulsory revisions:

Table 1:
Why were these parameters measured at 10 weeks and not 8 weeks. Since treatment started at 8 weeks, this is the baseline time point and not the 10 weeks.

We confirmed that these parameters were measured at 8 weeks. The mistake was corrected at Table 1.