

## **Point-by-point Response to Reviewers` comments for manuscript originally submitted as #74001:**

### **Referee #1:**

*The title reflect the scope of the study. It is well written and well expressed manuscript. The figures are well illustrated, but can the authors show the importance of aldosterone in the schematic figure 5? In addition, what are the limitations of the study?*

**Author response:** We thank this reviewer for the overall kind and positive comments about the quality of our work. The importance of aldosterone is illustrated in Fig. 5 by the listed toxic effects that its receptor, the MR, exerts on the myocardium. The limitations of our study are mentioned in “Discussion”. We hope this now satisfies this reviewer.

### **Referee #2:**

*Manuscript Title: GRK5 is an essential co-repressor of the cardiac mineralocorticoid receptor and is selectively induced by finerenone Manuscript Type: Basic Study Journal: World Journal of Cardiology Minor comments: The author appraised this manuscript by investigating potential differences between finerenone and eplerenone at engaging GRK5-dependent cardiac MR phosphorylation and subsequent blockade. However, your article is inadequately presented. Furthermore, there are many problems in the different sections as well. Although the article has scientific rigor, several minor flows need to be improved before publication. 1. The abstract section is unsuitable—no focus point in the abstract section.*

**Author response:** We also thank this reviewer for his/her overall kind and positive comments about our work. We have re-written the abstract to make it more focused.

*2. Rewrite the conclusion (in the abstract) in a more straightforward form. 3. In conclusion, finerenone, but not eplerenone, induces GRK5-dependent cardiac MR inhibition, which underlies, at least in part, its higher potency and efficacy, compared to eplerenone, as an MRA in the heart. GRK5 acts as a co-repressor of the cardiac MR and is essential for efficient MR antagonism in the myocardium. Change this.*

**Author response:** We also have re-written the conclusions according to the reviewer`s suggestion.

*4. Authors are suggested to use the full form when used for the first time throughout the manuscript.*

**Author response:** We also have re-written the conclusions according to the reviewer`s suggestion.

*5. The introduction section is poorly written. Authors are suggested to develop the introduction section by adding the literature related to finerenone.*

**Author response:** Done.

*6. The introduction section looks concise. Try to include the existing research limitations also, how the present research unravels those limits.*

**Author response:** Done.

*7. Need to arrange the introduction section logically—few updated references cited in this section.*

**Author response:** Done.

*8. Aim of the study need to write in the last paragraph of the introduction section.*

**Author response:** Ok.

*9. Material and methods are written without proper references. Need a logical flow of the writings with enough references.*

**Author response:** All pertinent references in “Materials and Methods” are provided.

*10. Luciferase Reporter Activity Assay: Need reference.*

**Author response:** Reference is provided (#11).

*11. Statistical Analyses: Need details.*

**Author response:** Done.

*12. The writing of results is good. Need to maintain a logical flow of the writings with the subtitles.*

**Author response:** Ok, thank you.

*13. Many grammatically problematic sentences are in the results and discussion section, which must be checked and corrected precisely.*

**Author response:** Done.

*14. Figures presentation is up to mark. 15. Figure legends are self-explanatory. 16. The discussion is feeble. Please, include the data from other sources about related works. 17. A sound discussion includes principal, relationship, and generalizations supported by the results. 18. In the discussion, many concepts already reported in the introduction are repeated, so it is better to avoid unnecessary repetitions.*

**Author response:** Done.

*19. The conclusion needs to address future perspectives.*

**Author response:** It does.

*20. Novelty of the work should be added by the author in the conclusion section.*

**Author response:** Done.

*21. Spacing, punctuation marks, grammar, and spelling errors should be reviewed thoroughly. I found so many typos throughout the manuscript.*

**Author response:** Done.

*22. English is modest. The authors need to improve their writing style. In addition, the whole manuscript needs to be checked by native English speakers.*

**Author response:** All authors (except for one) ARE native English speakers.

We hope now that the answers above have adequately addressed all of the reviewers' concerns and that the modifications we have introduced are satisfactory. We thank again all three reviewers for their constructive comments, which we strongly believe have substantially improved our manuscript.