

ESPS manuscript NO: 21861-manuscript, revised form

RESPONSE TO REVIEWERS:

Reviewer's code: 02745062

COMMENTS TO AUTHORS

"This is a perfect review."

Response to the Reviewer:

Thank you for the time spent in this matter and for your positive comments.

Reviewer's code: 00396997

COMMENTS TO AUTHORS

"This is well-written short review paper summarizing the recent updated information regarding the epigenetic modifications and microRNA-mediated gene regulation associated with the cardiovascular diseases and the strategies for clinical managements."

Response to the Reviewer:

Thank you for your observations. Your revision was helpful and improved the quality of the manuscript.

Major comments:

"1. Need to have extensive language editing. I will show the small examples in the minor comment section, but need to have careful proof reading across the whole manuscript. Please see the following minor comment section below."

Re: We followed your suggestions and we have revised the entire manuscript in both sentence structure and grammar, as well as syntax.

"2. Page 3 Line 5-7. "All these conditions may result in cardiomyocyte loss and in a cardiac remodeling with a consequent insufficient cardiac pump and increased risk of arrhythmias and heart failure (HF)". How about the cardiac fibroblast? Generally, it should have changes in non-cardiomyocyte cells also during the development of HF."

Re: We have modified and added the following sentences "All these conditions may result in cardiomyocyte loss and in a cardiac remodeling with a consequent heart failure (HF) and increased risk of arrhythmias and death. Also cardiac fibroblasts have a pivotal role in HF^[1]. Indeed, endothelial cell activation and inflammation promote the transdifferentiation of fibroblasts to myofibroblasts that after the extensive collagen production, the release of chemokines and the activation of inflammatory cells, causes in turn cardiomyocyte stiffness by contributing to pathogenesis of HF^[1]."

"3. Conclusion section. Conclusion section needs to be more conclusive and short. Need to takeoff the overlapping statements which are already described in the prior sections."

Re: As suggested we have rewired the Conclusion section removing overlapping statements already described

Minor comments:

"1. Page 2 line 8, "A lot of cardiovascular disorders". Change to "Numerous cardiovascular disorders"."

Re: As suggested we have changed the sentence "Numerous cardiovascular disorders are characterized by abnormal methylation....." instead of "A lot of cardiovascular disorders are characterized by abnormal methylation.....".

"2. Page 2 line 11, "antagomiR" Need to show the full form before using the abbreviation."

Re: We have shown the full form of "antagomiR" in the sentence "Indeed, large controlled trials are required to establish whether current possible candidate antisense microRNAs could offer better therapeutic benefits in clinical practice".

"3. Page 2 line 11-12, "offer a better therapeutic benefits". Take off "a"."

Re: We have taken off "a" from the sentence "Indeed, large controlled trials are required to establish whether current possible candidate antisense microRNAs could offer better therapeutic benefits in clinical practice.

"4. Page 3 line 4-5. "heart muscle (cardiomyopathy)". Change to "heart muscle (e.g. cardiomyopathy)"."

Re: As suggested we have changed "heart muscle (e.g. cardiomyopathy)" instead of "heart muscle (cardiomyopathy)".