Response to the Reviewer's Queries

Date: June 06, 2022

Manuscript Title: Role of cell-free DNA for predicting incidence and outcome of patients with ischemic stroke

Journal: World Journal of Neurology

Manuscript ID: 74913

On behalf of all the authors, I would like to thank all reviewers and editors for their constructive comments, which have helped us refine the manuscript. We are pleased to submit the revised manuscript for your kind perusal. The submission includes the following:

1. Response to reviewers' comments
2. Revised version of the manuscript (all changes are made in track version) **uploaded as Supplementary File** on submission portal
3. Figure as .ppt
4. Tables as .doc
5. Audio core tip
6. Copyright license agreement
7. Conflict of interest doc

We hope our responses to the reviewers' comments are satisfactory and believe that the revised manuscript is suitable for publication in your esteemed journal. Kindly find below the response to the reviewers' comments. We have made relevant changes to the manuscript.

S.No	Comments	Response to the Comments
Reviewer: 1		
1	This review discusses the potential utility of circulating DNA specifically cell-free mitochondrial DNA (cf-mtDNA) in determining the incidence and outcome of patients with ischemic stroke. However, the parts of Types of stroke Pathophysiological mechanisms of ischemic stroke，Major risk factors, Current management strategies are not necessary in this review, the topic of the review is the role of circulating DNA in ischemic stroke it is recommended to shorten this section.	Thank you for your valuable inputs! As suggested, we have shorten the sections and removed the non-relevant descriptions throughout the manuscript. We have also revised the whole manuscript mainly focusing on the role of cell-free DNA in ischemic stroke. Moreover, we have also cited few more relevant recent studies to explore more about the current progress in the field. We have also added section intensifying the discriminative quantification of cell-free nuclear and mitochondrial DNA for evaluating highly specific and sensitive tool for real-time non-invasive monitoring of disease diagnosis, prognosis, and exploring better therapeutic response.
Reviewer: 2		
1	Similar reviews discussing the association between DNA and stroke have been published, Cell-free DNA as a biomarker in stroke: Current status, problems and perspectives. The article lacks innovative arguments.	We agree with the reviewer's point of view; hence have added more recent reports describing the role of cell-free DNA while including the crucial involvement of cell-free mitochondrial DNA in ischemic stroke which has not been described properly till date. Furthermore, we have also added section intensifying the discriminative quantification of cell-free nuclear and mitochondrial DNA for evaluating highly specific and sensitive tool for real-time non-invasive monitoring of disease diagnosis, prognosis, and exploring better therapeutic response. Such investigations are rarely described in available literatures.
2	Too much description is devoted to the basics of stroke.	As per the suggestion, the basics of the stroke in introduction, stroke types, and pathophysiology sections have been shortened in this section. The current management strategy which is not well related to this article has been removed.
3	Core tips lack central ideas and main content.	The core tip has been revised, while focusing on the content of cell-free DNA as a biomarker and its importance in more sensitive diagnosis and prognosis of ischemic stroke.

Thank you again for consideration of our revised manuscript!

Sincerely,

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