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Rebuttal Letter (Point by Point response):

We are grateful for the valuable comments and suggestions from the editor and the reviewers on this manuscript. The rigorous review has helped us improving our manuscript. The reviewers' comments have been closely followed and revisions have been made accordingly. Please see below our point by point response.

Reviewer #1

1. Biostatistics: The manuscript does not provide specific information about biostatistics. It is recommended to include details on statistical methods and analyses if applicable.

Response: Thank you for reviewing our manuscript and for your valuable comments. The statistical analysis utilized in our study is mentioned in the “Materials and Methods” section. The statistical method of this study was reviewed by a professional biostatistician from Yarmouk University.

2. Ethics Statements: The manuscript did not provide information about ethics statements. Authors should submit formal ethics documents for review and approval.

Response: Thank you for your comment. The ethical approval was not needed for our study, since the human cell lines used were commercially purchased. This point is mentioned at the end of the manuscript and in the accompanying documents.

3. The limitations of the study are not explicitly stated. Authors should address any limitations, propose future directions, and highlight questions/issues that remain to be solved.

Response: Thank you for your valuable comment. We added the limitations of the study and future directions in the “Discussion” section.

Reviewer #2

1. The authors need to provide more detailed experimental steps and parameters so that other researchers can repeat the experiment.

Response: We would like to thank the reviewer for reviewing our manuscript and for this comment. We added the details of our experimental steps in the “Materials and Methods” section, so that readers could repeat the experiment.

2. In the results section, the authors need to describe the results in detail, including statistical methods and significance tests so that readers can better understand.

Response: Thank you for paying careful attention to these details. We included significance tests to the “Results” section for better understanding. Statistical methods are explained in more details in the “Materials and Methods” section.

3. The discussion section will need to explore the deep biological significance of the experimental results and how they compare to previous studies. At the same time, the authors also need to discuss the limitations of the experimental results and the direction of future research.

Response: Thank you for your valuable comment. We extended the “Discussion” section in order to add deeper details on the biological significance of the study results and how they compare to previous literature. We also added the limitations of the study and future directions in the “Discussion” section.

4. The language and writing are generally clear, but there are a few areas where clarification or edits would improve readability.

Response: We thank the reviewer for this comment. We corrected some sentences in the manuscript to improve readability and understanding.

5. The title seems incomplete and the authors can consider to perfect the title. I suggest that stress microenvironment be modified as stressful microenvironments.

Response: Thank you for this comment. We modified the title to be more specific and indicative of the contents of the study. The new title is: “Effects of high glucose and severe hypoxia on the proliferation, senescence and apoptosis of human adipose tissue-derived mesenchymal stem cells at various passages”. We changed “stress microenvironment” into “stressful microenvironments”, as suggested by the reviewer.

Note: all the changes are highlighted in yellow in the revised manuscript.