Reviewer’s report

Title: Effects of Early- and Mid-Life Stress on DNA Methylation of Genes Associated with Subclinical Cardiovascular Disease and Cognitive Impairment: A Systematic Review

Version: 0 Date: 14 Oct 2018

Reviewer: Nelson L.S. Tang

Reviewer's report:

The authors carried out a systemic review on an interesting area of human aging. The hypothesis of a role of DNA methylation in health related to human aging and other morbidity is an important area of research. 16 articles of both human and animal studies were covered. Epigenetic changes in NR3C1 gene among others were suggested to contribute to comorbidities during aging.

Those reviewed articles are relevant. Genes selected by each studies were described and results were evaluated.

However, there was a lack of elevation of the appropriate use of statistics in each of the reviewed studies. As there are different methods of analysis of epigenetic changes, each of them would need different statistical analysis. The authors should also review on this aspect so that the credibility of the results came from a particular study could be better appreciated.

These comments could append to the 2 tables.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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