

OPEN PEER REVIEW REPORT 1

Name of journal: Neural Regeneration Research

Manuscript NO: NRR-D-20-00132

Title: The Regulate Effects of Astaxanthin through Sirt1/ PGC-1 alpha signal pathway on Hippocampal Synaptic Protein in Aging Mice

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COMMENTS TO AUTHORS

It was not a high-quality study. However, addressing below questions may enable its fitting with the scope of the Neural Regeneration Research.

Main concerns

* The paper writes 'Nicotinamide (NAM) can inhibit the activity of Sirt1(Hwang ES et al.,2017;Pan S et al.,2019).' In cell culture, yes, extremely high level of NAM inhibits SIRT1. However, in animals (in view of high metabolism), NAM is also a precursor of NAD⁺ through the involvements of NAMPT and NMNAT1-3. Thus, NAM is not a good agent of SIRT1 inhibitor. Commonly used SIRT1 inhibitors are here

(https://www.scbt.com/browse/chemicals-Protein-Interacting-Inhibitors-Activators-Substrates-Protein-Inhibitors-SIRT1-Inhibitors/_/N-46rs9x)

* The paper writes '...intraperitoneally injected NAM (500 mol/L/d, purchased from sigma USA)'. Normally, we do 'injections (xxx mg NR/kg body weight)' since there are differences of the weights of the mice use. This reviewer has no idea how the authors did their work.

* Fig. 3, statistical values should be labelled in the Figure.

* Fig. 4, the data in B does not match with the 'representative blots' in A. E.g., changes of BDNF and PGC-1 α were not significant between the (Abeta +AST) and the (Abeta + AST + NAM) groups, while the quantitative data show there were big differences.

* For transparency as well as to provide additional information (e.g., numbers of samples and any data of outliers), dot blots should be added into Fig. 3 and Fig. 4B. This has been a mandatory standard for the Nature journals.

Minor concerns

* The paper writes 'Currently, oxidative stress is considered to be the leading cause of brain aging'. No, this reviewer does not agree with this (outdated) statement. Recently, 10 hallmarks of brain ageing were proposed and the authors were expected to revise their statements and to cite appropriate papers (PMIDs: 29874566; 31577933).

* Lines58-59 'ATP decreased(Maiti TK et al.,2015)'. A space is necessary before the reference. There are many such sloppy mistakes throughout the manuscript, and must be carefully addressed.