Review of: "Targeting Alzheimer's disease hallmarks with the Nrf2 activator Isoeugenol"

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Potential competing interests: No potential competing interests to declare.

Peer review: Targeting Alzheimer's disease hallmarks with the Nrf2 activator Isoeugenol

Thank you very much for inviting me to revise this article, and I'm sorry for the delay. This article is the first to demonstrate the beneficial effects of the Nrf2-activating molecule Isoeugenol in a preclinical model of Alzheimer´s disease, improving the outcomes of the main disease-associated hallmarks. The authors conducted this study both in vitro (in BV-2 cells exposed to LPS and N2a-APPswe) and in vivo (in the AD double transgenic mice APP/PS1) at an early (6-month-old animals) and late (11-month-old animals) AD stage with a large number of well-designed experiments. I have only some issues relative to both in vivo and in vitro experiments.

In vivo:

- The number of mice used in the study (5 APP/PS1 female mice) might be considered limited. Can the authors justify this choice?
- In the early AD stage experiments, the WT group treated with Isoeugenol is missing. Maybe I missed something, but I would like to know why this specific group is present in the late AD stage and not in the early one.

In vitro:

- No alterations were detected in Aβ42 peptide levels. Can the authors justify this result better in the discussion?

General comments:

- The authors should re-check the entire manuscript to correct any grammatical errors.
- The authors can improve the image quality and create a better figure for the experimental design to help the reader follow and summarize the consistent amount of experiments.
- The introduction is too long.