

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

Adriana Figueroa Garcia¹

¹ French Institute of Health and Medical Research

Potential competing interests: No potential competing interests to declare.

I must acknowledge the immense amount of work that has gone into this article. However, the English is rather confusing and I can't decipher the message it's trying to convey.

In the rest of the review, I have a few comments and suggestions for the authors.

Introduction

- The introduction is too long (3 pages), my advice is to cut it in half with a brief description of the pathology and what is known about treatment, and to highlight the mechanisms being studied and the importance of the study.

Materials and methods:

- First materials paragraph is not necessary. I think that there is no need to put every reagent in one paragraph, it could be just in the part dedicated to the specific method used. For antibodies, one recap table is enough and the same thing for the primers.
- Cell culture conditions are too detailed no need of the plate density or precise medium composition as you put the references of every reagent that has been used. Also serum decomplexation is implicit in cell culture don't need to mention it.
- A figure recapitulating the chronology of animal treatment and behavioural testing would be appreciated.
- Overall, there is a lot of elements that can be summed up and explained more briefly. If more details are necessary it can be put on Supplementary information.

Results

- The color code of the different conditions could be changed, it will facilitate the lecturer comprehension.
- Western blots figures are mostly cropped and sometimes no housekeeping gene is shown. I thought that the whole western blots would have been in the supplemental data but I can also find cropped blots.
- I don't think that the metabolic parameters of the mice are important for the paper per se, in fact the control of the parameters is important but there's no need to make a whole figure about it.
- What's more, pharmacokinetic studies of the molecule must be carried out prior to animal treatment.
- It's confusing to the lecturer the use of 6 mo females and 11 mo males in the materials and methods but then 11 mo females appeared on the results.

- In order to study the molecule's effect, it would have been interesting to see immunohistochemistry on amyloid plaques, microglial activation and even astrogliosis, since we're focusing on the brain. That will be complementary to AB levels measurement.
- 17 figures is too much, reduce the figures to only show the crucial data.
- **Nitrites** (instead of NO) production was measured in the supernatants of treated BV-2 cells [...]*n this paragraph to specify that this is an indirect measurement of NO. "inferred NO production".*
- **Fig. 5. Effect of Isoeugenol**The overall results strongly indicate that Iso has a potent anti-inflammatory role in a neuroinflammation context [...] Perhaps a little light on the assessment of inflammation and too "strong" a conclusion on the anti-inflammatory role of isoeugenol, a little more nuance would be appreciated...

Discussion

It's too long.

Conclusions

A summary diagram of the conclusions drawn at the end of this study would greatly assist understanding the article.