

## 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.

This work by Silva and co-workers is a commendable and well-conducted study.

I have a few recommendations regarding the analysis of Aβ40/Aβ42 inhibition:

- 1. Ensure consistency in referring to A $\beta$ 40 and A $\beta$ 42, whether using subscript or not (A $\beta$ 40 and A $\beta$ 42), as both forms are present in various sections of the text.
- 2. To enhance reader comprehension, consider including a concise explanation in either the introduction or discussion section about the functions and distinctions between A $\beta$ 40 and A $\beta$ 42. This is crucial for understanding their varying toxicity and aggregation properties. The absence of this clarification may leave readers without a clear understanding of why experiments are conducted on both isoforms, hindering the interpretation of results. For example, A $\beta$ 42 has a higher propensity for aggregation and is the primary component of amyloid plaques, making it a key target for aggregation inhibition. Isoeugenol demonstrated a reduction in the levels of only A $\beta$ 40 in N2A-APPswe cells, while affecting both A $\beta$ 40 and A $\beta$ 42 in mice. Providing this background information will assist readers in interpreting the obtained results.

I also suggest enhancing the text's readability by making it more concise, particularly in the Abstract, Introduction and Discussion sections.

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