

Review of “Glial Cell Involvement in Early Alzheimer’s Disease” by Rachel De La Torre. This manuscript describes a project assessing changes in synaptic architecture and the potential contribution of glial cells in a *Drosophila* model of Alzheimer’s Disease. Overall, the research project is well presented and the conclusions are appropriate and thoughtful. Some suggestions to improve the manuscript are provided below.

#1. The figures and legends in the Results sections are very nice, but some text should also be included in the Results. There is text embedded in the Discussion (for example, in the 3<sup>rd</sup> and 4<sup>th</sup> paragraphs of the Discussion) that could be moved to the Results. The Results should (briefly) state the experiments that you performed and your general findings/observations. The Discussion section then expands on the implications of your findings (what does it mean for others in your field; how would these results inform future experiments). I think the current Discussion is overall appropriate, but some description of the experiments/conclusions need to be included in the Results section.

#2. Some awkward sentences are noted below, with potential edits:

“It has been shown that developing mice deficient for one essential microglial engulfment receptor displayed immature and underdeveloped synaptic connectivity due to deficits in synaptic pruning (3,9).”

“Underdeveloped” is not the most appropriate description. Rather, these connections fail to become appropriately refined and thus are overabundant.

“Glial cells, the resident immune cells of the brain, are important for brain health as they represent a critical function both in brain injury as well as in brain development and maintenance.”

Glial cells, the resident immune cells of the brain, are important for brain health; they perform critical protective functions following brain injury, during nervous system development and to support general neuronal activity.

“Through this project, we hope to 1) determine similarities and differences between the *Drosophila* AD model and human disease, 2) identify glial signals that may contribute to synaptic loss in this model and 3) identify molecular targets, which can potentially be manipulated to prevent or delay the first signs of AD.”

I think these 3 major goals can be reframed to better match the findings of the project. For example, goal #1 (comparing fly AD model and humans) is not directly addressed in this work. After reviewing the results, I would propose that this project specifically addresses:

1. The effects of amyloid beta on synaptic molecule expression.
2. The contribution of Draper in amyloid beta-induced synaptic changes.

#3. Be sure to italicize “*Drosophila*” and all genes/transgenes, including *w*, *draper* and any transgene (e.g. *elav-Gal4*)

#4. Ensure that there is consistency throughout document referring to the amyloid beta harboring the arctic mutation. The abbreviation, italics, etc vary within the manuscript.