Examining the relationship between Nab2 overexpression and Tau abundance in a *D. melanogaster* neurodegenerative model

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Background

Neurodegenerative diseases that exhibit unusual Tau aggregation are referred to as tauopathies.

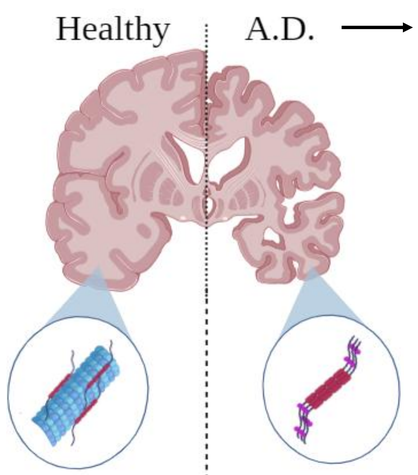


Figure 1.

Tau Becomes:

- Hyper-phosphorylated
- Aggregated
  - Forms NFTs
- Detached from microtubules

Contributing To:

- Microtubule loss
- Disruptions to cellular communication
- Cell death

Genetic Modifiers of Tauopathy Pathology

Certain genes can alter the severity or symptoms of a disease when expressed in various ways.

Decreased protein production | ~ Elimination of protein production | Increased protein production

⇧ ZC3H14 (mammals) → increased disease-related tau accumulation (Wheeler et al., 2019)

Modeling Tauopathy in *Drosophila melanogaster*

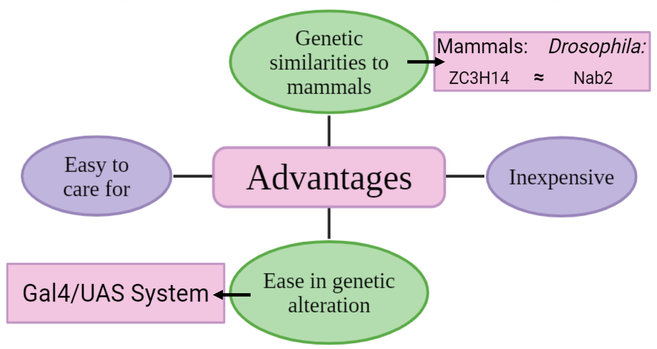


Figure 2. Advantages of using *Drosophila* as a model system.

⇧ Nab2 *(Drosophila)* → decreased Tau abundance? (Yim 2020)

Question and Hypotheses

Does Nab2 overexpression affect Tau abundance in a tauopathy model of *Drosophila*?

1. Flies overexpressing both Nab2 and Tau will contain less Tau than flies only overexpressing Tau.
2. Unique dosages of Nab2 overexpression will distinctly influence Tau abundance in *Drosophila.*

Methodology

1. Lysis and Sample Prep
2. Electrophoresis and Transfer
3. Incubate with 1° and 2° antibodies
3. Develop and Visualize

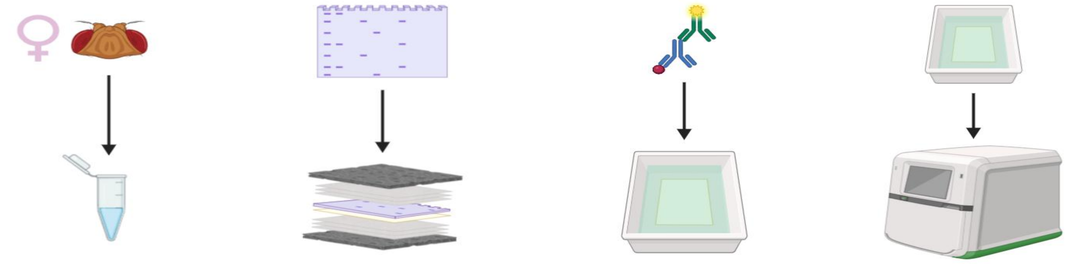


Figure 3. Immunoblotting procedure to detect Tau and/or Nab2 abundance in different fly conditions

Results and Conclusions

Figure 4.

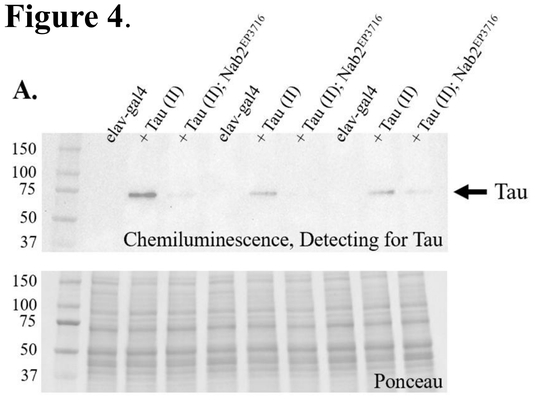
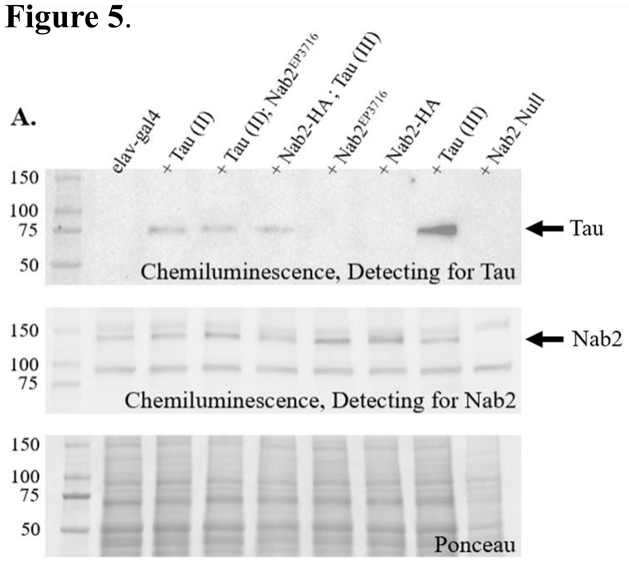


Figure 4. Overexpression of Nab2 has no significant effect on Tau abundance.

A non-significant trend showed that flies overexpressing Tau and Nab2 contained less Tau than flies only overexpressing Tau ($p = 0.08$)

Substantial variation in protein abundance was present across condition replicates

Figure 5.



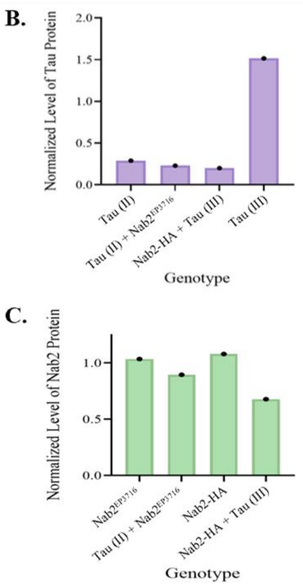


Figure 5. Overexpression of Nab2-HA appears to decrease Tau abundance.

Nab2 overexpressing conditions contained visibly more Nab2 than corresponding Tau + Nab2 conditions

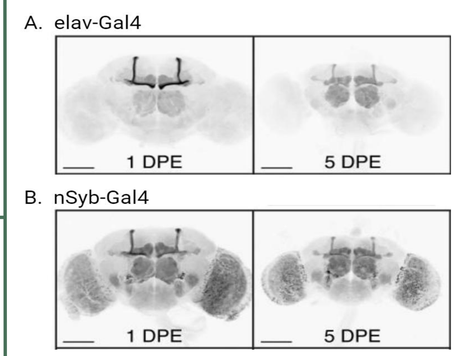
Notes:

A. No statistical analysis can be completed with zero-replicate data

B. I was unable to address hypothesis #2 because Nab2-HA and Nab2^{EP3716} appeared to produce similar levels of Nab2 (Figure not included)

Future Endeavors

1. Investigate other ways to overproduce Tau/Nab2 in neurons.
   - Will this help mitigate protein abundance variation across replicates?



(**Figure 6;** Delandre et al., 2025)

2. Investigate whether Nab2 abundance is impacted by changes to Tau expression.

Citations

Chee et al. 2005, *Neurobiology of Disease*, *20*(3), 918–928.
Cowan et al., 2010, *Acta Neuropathologica*, *120*(5), 593–604.
Delandre et al., 2025, *Genetics*, *229*(3)
Wheeler et al. 2019, *Science Translational Medicine*, *11*(523)

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