

# Using Drosophila to Study Alcohol Use Disorder (AUD) From Human GWAS

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## Background

Alcohol use disorder (AUD) is a medical condition that affects 1 in 10 Americans aged 12 and older. Analysis of human Genome-wide association studies (GWAS) have uncovered 43 candidate genes of interest that might influence AUD related traits, in which 37 are shared in Drosophila. The purpose of this project is to use the fruit fly model to test which of these genes is relevant for alcohol-related behaviors *in vivo*, and correlate studies of flies with humans by understanding the genetic component of AUD that may put people at risk.

Overall goal: Use Drosophila to study alcohol use disorder (AUD) and alcohol consumption by integrating multiple GWAS with 3D genomics-based methods

## Methodology

- 3D genomics will identify single-nucleotide polymorphisms (SNPs) residing in open chromatin
- Knock down the fly orthologs of these genes and conduct ethanol behavioral assays on each line
- Alcohol related behavior in flies can be used to inform on more complex behaviors in humans related to AUD.

## Conducting the Ethanol Behavioral Assay

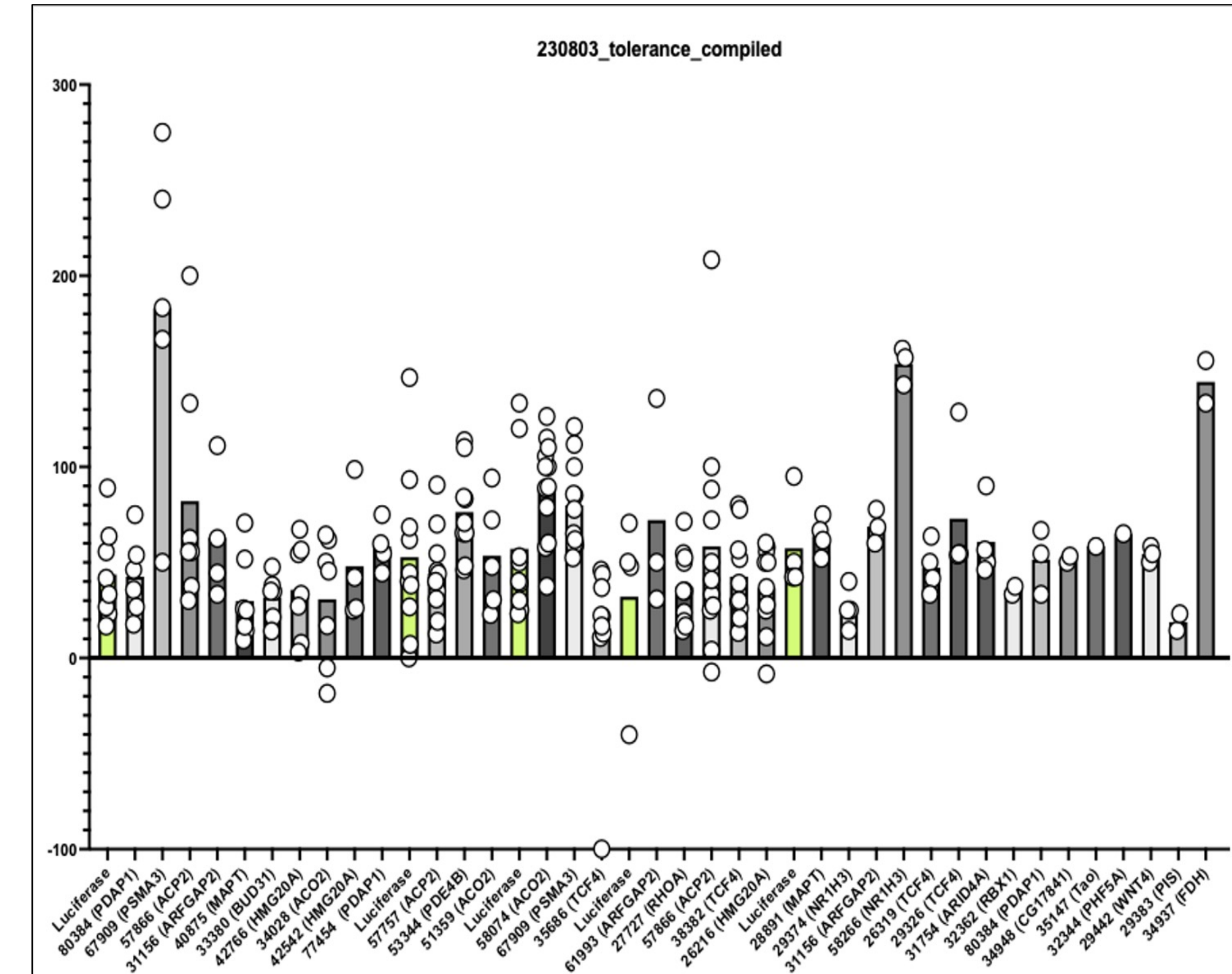
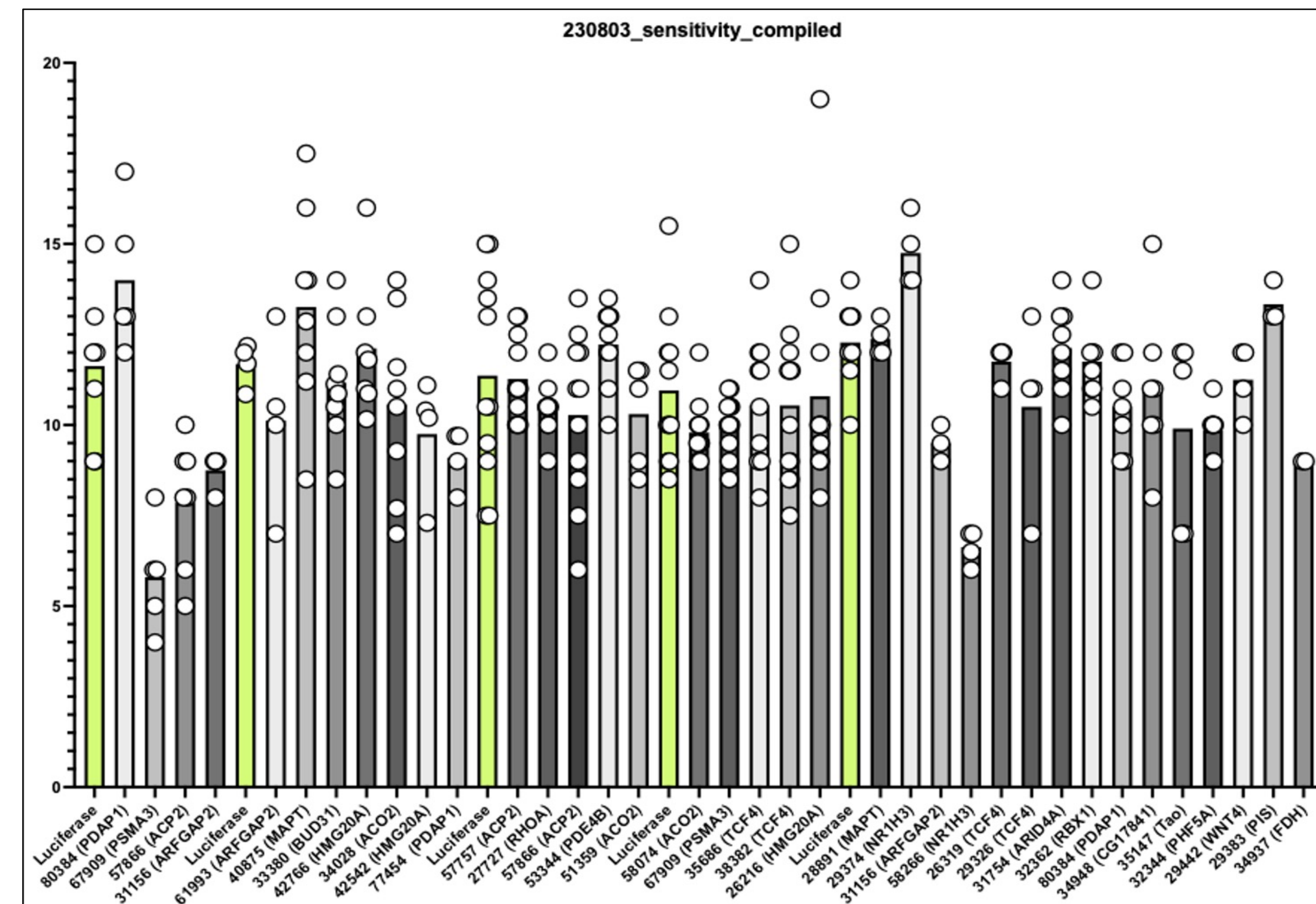
- Ethanol behavioral assay
  - Exposing the flies to 5 ml of ethanol in vials twice over a period of 4 hours
  - Monitoring their mobility as a response to sedation
  - Measuring sensitivity and tolerance

## Sensitivity and Tolerance using the Median Sedation Time (MST)

- Use Median Sedation Time (MST) to measure sensitivity, which is the initial response time to ethanol exposure till the flies are sedated
- Monitoring Mobility: flies are sedated when they have been stationary and unable to turn themselves over
- Tolerance - a reduction in the response to alcohol following a pre-exposure to alcohol

\*This project tested rapid tolerance, which is tolerance built up over one drinking session. Humans experience chronic tolerance following repeated/continuous alcohol consumption over a longer period of time

## Results



## Future Considerations

- Potential Lines of Interest
  - 67909
    - Alpha 7
    - ATP dependent proteasome
  - 58266
    - Protein coding gene
    - Ortholog to human C1NP (cyclin dependent kinase 2 interacting protein)
  - 34937
    - Associated with protein coding gene

Next steps:

In the future, a potential route could be to target the stage in development that the potential genes function in and assessing the neurons/pathways that they affect.