CHRD 2024: Abstract Submission Form

Presenter Name
Anthony Kozak

Presenter Status
Masters Student

Role in the project
Perform Experiments
Analyze Data
Write Abstract

Research Category
Basic Science

Title
Genetic Screen of Conserved 22q11.2 Genes in Neurons and Glia Using Drosophila melanogaster

Background
22q11.2 deletion syndrome (DS) affects 1 in 1000-6000 births and is a highly heterogenous genetic condition. 22q11.2 DS causes a wide range of symptoms including, but not limited to autism spectrum disorder, attention deficit hyperactivity disorder, schizophrenia, and seizures. Little is known about which 22q11.2 genes are important in the pathogenesis of 22q11.2 DS.

Objective
Since 22q11.2 DS is typically caused by de novo non-homologous meiotic recombination events, we hypothesize that 22q11.2 DS phenotypes are largely caused by haploinsufficiency of a fraction of 22q11.2 genes (critical genes). Our objective is to find these critical 22q11.2 genes.

Methods
This unbiased genetic screen is based on RNAi-mediated knockdown of 22q11.2 DS gene orthologues in neurons or glia using the UAS-GAL4 system in Drosophila melanogaster. First, when flies eclose, mendelian ratios are calculated to assess lethality from RNAi-induced knockdown of target genes. Second, flies are aged to day 20 with any fatalities being recorded. Then, flies were assessed on their ability to climb in a straight line. Finally, flies are vortexed to assess susceptibility to mechanically induced seizures.

Results
In neuronal knockdown, to date, we have identified eight lethal genes, three genes causing locomotion defects, and four genes which increase the flies' susceptibility to mechanically induced seizures. In glial knockdown, we have identified eight lethal genes, five genes causing locomotion defects, and five genes which increase the flies' susceptibility to mechanically induced seizures.

Conclusion
Our results support our hypothesis that only a subset (19/31) of the conserved genes knocked down in the brain cause a phenotype. Identifying these critical genes in Drosophila may be used as justification for knocking down the orthologous genes in a mammalian model, or for studying whether upregulation causes amelioration of the phenotypes. A limitation of our study is that it examines each gene in isolation. Future studies will examine gene interactions.

Do you have a table/figure to upload?
No

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