Presenting Author Name
Delaram Jebreili Rizi

Presenting Author Category
Masters Student

Research Category
Basic Science

Abstract Title
Modelling SYNGAP1-Related Disorders and Variant Function in Drosophila melanogaster

Background
De novo SYNGAP1 variants cause childhood neurodevelopmental conditions, including Intellectual Disability, Autism Spectrum Disorder, epilepsy and behavioural difficulties. These phenotypes align with SYNGAP1's role in postsynaptic signalling.

Objective
The functional impact of patient-specific variants remains poorly understood, and a Drosophila model has yet to be established.

Methods
We generated transgenic flies expressing human SYNGAP1 and 16 disease-associated variants, including both truncating and missense changes. By crossing these with tissue-specific GAL4 drivers, we overexpress SYNGAP1 to identify any phenotypes and compare variant functions. In parallel, we are studying the SYNGAP1 ortholog in Drosophila, raskol. Using RNAi, we knocked down raskol in either neurons or glia and assessed lethality, lifespan, climbing, and seizure behaviour. Finally, using a germline mutant, raskolTG4, we will humanize with our UAS-SYNGAP1 transgenes to rescue phenotypes and assess variant function.

Results
Our preliminary data indicate that overexpression of the UAS-SYNGAP1 reference does not produce visible eye or wing abnormalities. Also, knockdown of raskol causes minimal phenotypes but may induce heat-induced seizures.

Conclusion
Overexpression of human SYNGAP1 was well tolerated without visible abnormalities, suggesting that SYNGAP1 gene therapy may be safe and help mitigate symptoms. By contrast, raskol knockdown produced no robust phenotypes, suggesting that raskol may not play as critical a role in the fly nervous system as human SYNGAP1 under the conditions assayed. Establishing raskol loss-of-function models and systematically testing patient-derived variants in flies will deepen insight into genotype–phenotype relationships and disease heterogeneity, laying the groundwork for future therapeutic screens with potential clinical relevance.

Authors

Name	Role	Profession
Delaram Jebreili Rizi	Presenting Author	Graduate
Yina Her	Co Author	Graduate
Paul C. Marcogliese	Co Author	Assistant Professor