CHRD 2024: Abstract Submission Form

Presenter Name
Delaram Jebreili Rizi

Presenter Status
Masters Student

Role in the project
Design
Perform Experiments
Analyze Data
Write Abstract

Research Category
Basic Science

Title
Understanding SYNGAP1 Using Drosophila melanogaster

Background
SYNGAP1 encodes a synaptic Ras-GTPase-activating protein expressed mainly in the synapses of excitatory neurons. De novo variants in SYNGAP1 cause neurodevelopmental conditions in children (MIM *603384), including Intellectual Disability (ID), Autism Spectrum Disorder (ASD), schizophrenia, and epilepsy. Most affected individuals show a range of developmental delay, motor and speech impairment, and some develop seizures, consistent with SYNGAP1's function in postsynaptic signalling and dendritic spine maturation. However, the impact of patient-specific variants on protein function is lacking.

Objective
We aim to study SYNGAP1 by examining its Drosophila ortholog, raskol, in neurons and glia in the developing nervous systems, and by expressing human SYNGAP1 and patient variants in flies to explore genotype-phenotype correlations, as well as the heterogeneity of SYNGAP1-related conditions.

Methods
We have generated the first transgenic flies that express human SYNGAP1 and 19 disease variants by using site-directed mutagenesis and commercial transgenesis. We will cross these flies with various tissue-specific GAL4 drivers to overexpress SYNGAP1 in different tissues, such as the eye and wing, and examine any abnormal phenotypes. Additionally, we knockdown raskol by using three independent RNAi and employ pan-neuronal (nSyb-GAL4) and pan-glial (Repo-GAL4) drivers to investigate the function of raskol in these tissues and examine lethality, lifespan, climbing, and seizure behaviour in different temperatures.

Results
We have successfully generated UAS plasmids containing SYNGAP1 reference and 17/19 of the patient-specific variants. They will now be microinjected into embryos for transgenesis. Our preliminary data indicates that 2/3 independent raskol RNAi lines cause minimal phenotypes in flies aged to 20 days. However, one RNAi line causes lethality when expressed in glia and semi-lethality when expressed in neurons.

Conclusion
SYNGAP1 is a critical gene in neurons. Our data, although preliminary, indicates it may have a conserved function in glia. Future experiments will confirm this and determine the impact of the variants generated.

Do you have a table/figure to upload?
No

Authors

Name	Email	Role	Profession
Delaram Jebreili Rizi	jebreild@myumanitoba.ca	Presenting Author	Graduate
Yina Her1	hery@myumanitoba.ca	Co Author	Graduate
Paul C. Marcogliese	paul.marcogliese@umanitoba.ca	Co Author	Assistant Professor