Presenting Author Name
Yina Her

Presenting Author Category
Masters Student

Research Category
Basic Science

Abstract Title
Characterizing the Neuronal Role of CK2 Using Drosophila melanogaster

Background
De novo variants in either CSNK2A1 or CSNK2B cause neurodevelopmental disorders with overlapping features and variable symptoms. These two genes encode subunits of the Casein Kinase 2 (CK2) complex. CK2 is enriched in the central nervous system and is believed to be constitutively active. Currently, there are no in vivo models in flies to study CK2 in the adult central nervous system. Moreover, the variants, particularly missense, found in CSNK2A1 or CSNK2B have yet to be functionally assessed in vivo.

Objective
There are three objectives of this study. First, we will determine CK2 function in the nervous system of flies, in both brain cells (neurons). Our preliminary data reveal that neuronal CK2 is critical for most flies to reach the adult stage, with surviving flies having wing defects and shortened lifespan. CK2 is expressed in adult humans and flies. We will conduct adult-specific reduction of CK2 in neurons and determine whether flies display movement deficits and/or seizure-like behaviour. Secondly, we will also express the human versions of CSNK2A1 and CSNK2B, including the disease-causing variants, in fruit flies to determine if variants act differently. Finally, since CK2 is a Wnt agonist, we will test drugs that increase the Wnt signalling pathway in our fly models. This work will shed insight into CK2 function in the brain, the consequences of patient variants, and determine therapeutic leads.

Methods
CK2 (CkIIα and CkIIβ) are knocked down in Drosophila neurons by RNAi using the nSyb-GAL4 driver for initiating knockdown during development and elav-GAL4GS for adult-specific knockdown. Drosophila behavioural assessment was performed by negative geotaxis. Seizure induction was performed by the bang-sensitivity assay. Variant transgenic flies were generated via site-directed mutagenesis, followed by Sanger verification, and embryo injection commercially.

Results
We found that neuronal knockdown of either CkIIα or CkIIβ in neurons with nSyb-GAL4 resulted in lethality, where some escapers had wing defects. No obvious phenotype was observed with elav-GAL4. We successfully generated 16 variants in CSNK2A1 or CSNK2B to generate transgenic flies. Tissue-specific overexpression using nub-GAL4 and ey-GAL4 showed defects in wings in the variants.

Conclusion
We have been able to establish that neuronal CK2 is critical for the development of Drosophila melanogaster. Future studies will examine the adult-specific role of CK2 in neurons. Our variant functional testing is revealing a wide variety of variant impacts.

Authors

Name	Role	Profession
Yina Her		Masters student
Danielle Pascual		PhD student
Harsimran Kaur		Lab Tech
Catherine Bland		
Paul Marcogliese		Assistant Professor