

Presenting Author Name

VASHNAVI VASHIST

Phonetic spelling of your (full) name

Vaishnavi Vaishist

Presenting Author Category

Masters Student

Supervisor Name

Paul Marcogliese

GBD Audio File

WhatsApp Audio 2026-09-03 at 1.42.39 PM.mp4

Headshot

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Short Bio (100 words)

Vashnavi is a graduate student in Biochemistry and Medical Genetics at the University of Manitoba. She completed her Bachelor of Science in Biomedical Science at Capilano University, where she developed a strong interest in genetics and cell biology. Her undergraduate research focused on RNAi knockdown of the daf-2 gene in *C. elegans* to study lifespan modulation. Her current research uses *Drosophila melanogaster* to model neurodevelopmental disorders associated with KAT6A and KAT6B variants. Outside of research, she tutors high school students and enjoys portrait sketching, painting, henna art, cooking, and crafts.

Research Category

Basic Science

Abstract Title

Variant Function and Disease Modelling related to KAT6A and KAT6B Neurodevelopmental disorders in *Drosophila melanogaster*.

Authors

Name	Role	Profession
Vashnavi Vashist	Presenting Author	Graduate
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Background

KAT6A and KAT6B encode lysine acetyltransferases that play important roles in histone acetylation and transcriptional regulation. De novo pathogenic variants in KAT6A are linked to Arboleda-Tham syndrome (ATS), while pathogenic variants in KAT6B are associated with Genitopatellar syndrome (GPS) and Say-Barber-Biesecker-Young-Simpson syndrome (SBBYSS). However, there is substantial clinical heterogeneity. Early truncations are known to cause haploinsufficiency, while late C-terminal truncations are clinically more severe, although a dominant-negative or gain-of-function mechanism has not yet been demonstrated. Many missense variants remain variants of uncertain significance because their functional impact is unknown, limiting diagnosis.

Objective

To investigate the functional effects of pathogenic and uncertain KAT6A and KAT6B variants and determine whether different variant classes exhibit distinct loss-of-function, gain-of-function, or dominant-negative behaviours.

Methods

We used *Drosophila melanogaster* as a model organism. Using the GAL4/UAS system, variant effects were assessed with ubiquitous and tissue-specific drivers. Phenotypic outcomes, including lethality, Mendelian ratios, and wing morphology, were used to classify functional impact. In parallel, we examined the role of the single KAT6A/B ortholog, *enok*, in *Drosophila* neurons and glia.

Results

Most truncating pathogenic variants exhibited loss-of-function behaviour, consistent with haploinsufficiency. However, C-terminal truncations behaved differently and showed evidence of a potentially dominant-negative mechanism. In contrast, KAT6A missense variants showed gain-of-function behaviour, whereas KAT6B missense variants predominantly displayed loss-of-function behaviour.

Conclusion

These findings reveal distinct, variant-specific mechanisms of pathogenicity in KAT6A and KAT6B. The results emphasize the importance of functional assays for interpreting disease-associated variants and may improve our understanding of the molecular mechanisms underlying KAT6-related neurodevelopmental disorders.