

## A null mutation of *C. elegans vwa-8*

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**Figure 1:** (A) shown is *vwa-8* gene structure from WormBase (Version: WS276). Blue bar indicates *vwa-8(ju1659)* deletion. (B) *vwa-8(ju1659)* deletes 7989bp. The start and stop codons of the F11C1.5a.1 isoform are highlighted in yellow. Exonal sequences are shown in uppercase.

### Description

VWA8 proteins, named for von Willebrand factor A (VWA) domain containing 8, are conserved from worm to mammals (Whittaker & Hynes, 2002). In human, two SNPs (rs9566845 and rs9566867) in *vwa8* are found to be associated with bipolar disorder with comorbid migraine (Oedegaard *et al.*, 2010). Another SNP (rs9532931) is tentatively associated with a specific sub-group of autism patients (Anney *et al.*, 2010). The *C. elegans* VWA-8 long isoform shares 38% and 55% amino acid sequence identity and similarity, respectively, with human VWA8 long isoform. We showed that endogenous VWA-8 is expressed in mitochondria of somatic tissues, except neurons (Zhu, Chisholm & Jin, 2020). To determine the function of *C. elegans vwa-8*, we generated a null allele *vwa-8(ju1659)* by CRISPR-Cas9. *vwa-8(ju1659)* mutants are homozygous viable, and indistinguishable from wild type in gross phenotypes such as body size, brood size, growth rate and movement.

### Methods

We generated *vwa-8(ju1659)* using two CRISPR RNA (crRNAs), 5'-AGTGAAACCCGTGTGATCAT-3' and 5'-CTACAACGAGAGTTGCCTGT-3' (Integrated DNA Technologies) targeting the start and stop codons of *vwa-8*, respectively. The crRNAs were injected into wild type hermaphrodites with purified Cas9 protein (MacroLabs, University of California Berkeley), trans-activating crRNA (tracrRNA) and *dpy-10* crRNA, as described (Paix, Folkmann, Rasoloson, & Seydoux, 2015). The dumpy F1 progeny of the injected P0 wild type animals were singled to separate plates. F1 dumpy worms were then genotyped for the presence of potential *vwa-8* deletions using the following primers: 5'-CCTCGAGGGCCCCATATTTT-3' and 5'-TGCTCTCGAACACCTTGCTT-3'. Several independent *vwa-8* deletions were identified. All deletion mutants behaved similarly. *ju1659* is a 7989bp deletion of *vwa-8* which removes nearly all the coding sequence of *vwa-8*, except the last 82bp of the last exon. CZ26606 *vwa-8(ju1659)* was generated after outcrossing with N2 for 3 times to remove the dumpy mutation.

### Reagents

CZ26606 *vwa-8(ju1659)* will be available at the CGC.

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### References

Anney, R., Klei, L., Pinto, D., Regan, R., Conroy, J., Magalhaes, T. R., . . . Hallmayer, J. (2010). A genome-wide scan for common alleles affecting risk for autism. *Hum Mol Genet*, 19(20), 4072-4082. DOI: 10.1093/hmg/ddq307 | PMID: 20663923.

Oedegaard, K. J., Greenwood, T. A., Johansson, S., Jacobsen, K. K., Halmoy, A., Fasmer, O. B., . . . Kelsoe, J. R. (2010). A genome-wide association study of bipolar disorder and comorbid migraine. *Genes Brain Behav*, 9(7), 673-680. DOI: 10.1111/j.1601-183X.2010.00601.x | PMID: 20528957.

Paix, A., Folkmann, A., Rasoloson, D., & Seydoux, G. (2015). High efficiency, homology-directed genome editing in *Caenorhabditis elegans* using CRISPR-Cas9 ribonucleoprotein complexes. *Genetics*, 201(1), 47-54. DOI: 10.1534/genetics.115.179382 | PMID: 26187122.

Whittaker, C. A., & Hynes, R. O. (2002). Distribution and evolution of von Willebrand/integrin A domains: widely dispersed domains with roles in cell adhesion and elsewhere. *Mol Biol Cell*, 13(10), 3369-3387. DOI: 10.1091/mbc.e02-05-0259 | PMID: 12388743.

Zhu, M., Chisholm, A.D., Jin, Y. (2020). *C. elegans* VWA-8 is a mitochondrial protein. *microPublication Biology*. DOI: 10.17912/micropub.biology.000264

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