

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

Ming Zhu<sup>1</sup>, Andrew D Chisholm<sup>1</sup> and Yishi Jin<sup>1§</sup>

<sup>1</sup>Section of Neurobiology, University of California San Diego, La Jolla, CA 92093, United States

<sup>§</sup>To whom correspondence should be addressed: yijin@ucsd.edu



**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

[Request a detailed protocol](#)

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.

**Acknowledgments:** We thank members of the Jin and Chisholm laboratories for valuable discussions. We acknowledge WormBase as an information resource.

## 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

**Funding:** This work was supported by NIH R01 NS093588 to AC and YJ and R01 GM054657 to AC.

**Author Contributions:** Ming Zhu: Investigation, Writing - original draft, Writing - review and editing. Andrew D Chisholm: Funding acquisition, Supervision, Writing - review and editing. Yishi Jin: Funding acquisition, Supervision, Writing - review and editing.

**Reviewed By:** Anonymous

**History:** Received May 20, 2020 **Revision received** June 1, 2020 **Accepted** June 2, 2020 **Published** June 7, 2020

**Copyright:** © 2020 by the authors. This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International (CC BY 4.0) License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

**Citation:** Zhu, M; Chisholm, AD; Jin, Y (2020). A null mutation of *C. elegans vwa-8*. *microPublication Biology*. <https://doi.org/10.17912/micropub.biology.000263>