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’-AGTGAAACCGTGACCGGTTT…AACATTGCTCAATAGTgaactttt… and 5’-CTACAAGGAGTTTTGTTTTAAAAGACCTTCTTAGGC… TTCGAAAAAAAAT…TGAAGACCACTTCTCATCAACTATTGCTCAATTAGTgaactttt… 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’-CCTGAGGAGCCCATATT…TGTGACTGAAACACCTTG…TTT-3’ and 5’-CTACACAGGAGGTGCCTG…TCCG…GTAC-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**

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