C44B9.1 Is a Novel Conserved Neuronal Protein Likely Involved in Synaptic Vesicle Exocytosis

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We are interested in the regulation of locomotion and its modulation by environmental signals. Wild-type animals decrease their speed by 70% when they encounter a bacterial lawn after brief food deprivation. Animals lacking MOD-5, a serotonin reuptake transporter (SERT), reduce their speed by more than 90% upon reaching bacteria after being briefly food-deprived but show close to normal locomotion off food. We screened for modifiers of the *mod-5(n3314)* phenotype to identify new mutations that affect the modulation of locomotion. Such modulators of locomotion might have been missed in previous screens that did not use sensitized backgrounds seeking locomotion-impaired animals.

We mutagenized *mod-5* animals and isolated potential *mod-5* enhancer mutations that caused *mod-5* worms to nearly paralyze on bacteria after being briefly food-deprived. Two non-complementing alleles, *n3925* and *n4022*, were found to be nonsense mutations in the uncharacterized gene *C44B9.1*. Mutations in *C44B9.1* cause a severe locomotion defect on food even when separated from *mod-5(n3314)*. *C44B9.1* encodes a novel protein with no known functional domains and is conserved from *C. elegans* to humans. We built a transcriptional *GFP* reporter for *C44B9.1* and found that it is expressed in most non-pharyngeal neurons.

The *n4022* strain shows decreased sensitivity to aldicarb, an acetylcholinesterase inhibitor, and increased sensitivity to levamisole, an acetylcholine receptor agonist, suggesting a presynaptic role for *C44B9.1*. In addition to their locomotion defect, *C44B9.1* mutants retain eggs *in utero* for an abnormally long period of time, which leads to eggs being laid at a later developmental stage. The phenotype and drug sensitivity profile of *C44B9.1* animals are similar to those of strains mutant in genes involved in the regulation of synaptic vesicle exocytosis, such as *unc-64* (syntaxin), *unc-31* (CAPS), and *aex-3* (a RAB-3 GEF).

We are currently investigating the interactions of *C44B9.1* with genes involved in neurotransmission, performing suppressor screens, and using biochemical assays to identify physical partners of C44B9.1. We plan to use optogenetics and electrophysiology to assess the role of *C44B9.1* in synaptic vesicle exocytosis and cell excitability.

Poster
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