The Novel Conserved Gene *C44B9.1* Regulates *C. elegans* Behavior through G Protein Signaling and Likely Regulates Synaptic Vesicle Release

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C. elegans modulates its locomotion and egg-laying behavior in response to environmental signals and its past feeding experience. For example, after encountering food animals slow their locomotion and lay eggs. In the absence of food, worms increase their locomotion and refrain from laying eggs. Animals that have been well-fed slow their locomotory rates when they encounter food (a behavior termed the "basal slowing response") less than do animals that have been food-deprived (termed the "enhanced slowing response"), presumably because food-deprived animals have a greater need for staying in the proximity of food.

We performed a mutagenesis screen and isolated mutations that cause well-fed animals to behave as if they had been food-deprived, thus modifying their behavioral state by uncoupling the extent of food-dependent slowing from past feeding experience. We isolated alleles of an uncharacterized gene that is highly conserved from *C. elegans* to humans, *C44B9.1*. Mutations in *C44B9.1* cause a severe locomotion defect of well-fed animals in the presence of food but have little effect on the locomotion of well-fed animals in the absence of food. Well-fed *C44B9.1* mutant animals also lay eggs at abnormally late developmental stages, as if they had been food-deprived. *C44B9.1* is expressed in most if not all neurons and is possibly neural-specific. The pharmacological sensitivity profile of *C44B9.1* mutant animals suggests a presynaptic role for *C44B9.1*. The behavioral phenotype and drug-sensitivity profile of *C44B9.1* animals are similar to those of mutants with defects in the regulation of synaptic vesicle exocytosis, such as *unc-64* (syntaxin) and *unc-31* (CAPS), suggesting that *C44B9.1* might regulate synaptic vesicle release. The C44B9.1 protein localizes to synapse rich-areas of neuron processes. Like synaptic vesicles, C44B9.1 fails to be transported and accumulates in neuronal cell bodies of animals mutant for the kinesin-like protein UNC-104/KIF1A. *C44B9.1* mutations suppress the egg-laying constitutive defect of mutants of the Gαo gene *goa-1* and its downstream effector diacylglycerol kinase gene *dgk-1*, suggesting that *C44B9.1* functions downstream of or in parallel to this inhibitory G protein signaling pathway. In short, these results suggest that *C44B9.1* and possibly its homologs are regulators of synaptic vesicle release.

We are currently investigating the pathway in which *C44B9.1* functions and identifying physical partners. In addition to characterizing a conserved protein likely involved in synaptic vesicle release, these studies of *C44B9.1* might also define a genetic pathway that regulates behavioral states associated with food experience.

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