

## FLP-18 Neuropeptide Signaling Functions to Increase *C. elegans* Body Curvature

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The *C. elegans* genome contains a large family of *flp* genes, which encode FMRFamide-related peptides. However, the functions of these neuropeptides are poorly understood. We studied the neuropeptide gene *flp-18* by using its overexpression phenotype as an *in vivo* assay for peptide activity. Overexpression of *flp-18* shortened body length, increased body curvature, decreased velocity and caused uncoordinated reverse locomotion. We sought suppressors of the behavioral defects caused by *flp-18* overexpression by testing candidate genes and by mutant screens. We found that the G protein-coupled receptor gene *Y58G8A.4* is required for the body length and posture defects of *flp-18* overexpressors, suggesting that Y58G8A.4 mediates the control of body shape by FLP-18 signaling. Overexpression of *Y58G8A.4* caused the same behavioral defects as overexpression of *flp-18*. The receptor overexpression phenotype was suppressed by deletion of *flp-18*, indicating that Y58G8A.4 receptor activity is regulated by FLP-18 peptides *in vivo*.

Because *flp-18* deletion mutants were grossly wild-type we tested whether FLP-18 peptides function redundantly with small-molecule transmitters. Specifically, we examined animals multiply mutant for *flp-18* and genes required for the synthesis or transmission of acetylcholine, GABA, tyramine and octopamine or serotonin. We found that deletion of *flp-18* partially suppressed the increased-curvature defect of *cha-1* and *unc-29* mutants, which have decreased cholinergic signaling, suggesting that one function of FLP-18 is to increase curvature.

To identify cellular circuits that use FLP-18 peptides to control posture, we generated a functional *flp-18::gfp* reporter transgene. We observed expression of *flp-18::gfp* in head neurons, approximately a dozen neurons in the ventral nerve cord, the dorsal nerve cord and one tail neuron. *flp-18::gfp* was coexpressed with a cholinergic marker in some ventral nerve cord motor neurons, but not in head or tail neurons. A functional *Y58G8A.4::gfp* reporter gene was expressed primarily in body-wall muscles. These expression patterns suggest that FLP-18 peptides regulate body curvature by acting directly on body-wall muscles and might be released from cholinergic ventral cord motor neurons.

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