A FMRFamide Neuropeptide Signaling Pathway and Acetylcholine Negatively Regulate C. elegans Egg-laying Behavior

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C. elegans egg laying involves a simple motor program that is modulated by the animal's environment and experience. To identify molecular pathways that regulate C. elegans egg-laying behavior, we are characterizing genes that when mutated cause severe egg-laying defects but do not strongly affect muscle or motor neuron function by pharmacological criteria. We have positionally cloned one such gene, egl-6, defined by a single gain-of-function allele, n592, and found that egl-6 encodes a receptor for the FMRFamide neuropeptides FLP-10 and FLP-17. Increased dosage of egl-6, flp-10 or flp-17 causes strong egg-laying defects. By contrast, deletion of egl-6, flp-10 or flp-17 does not cause obvious defects in egg-laying behavior, suggesting that this neuropeptide signaling pathway might function redundantly with another signal to inhibit egg laying.

We have tested whether any known neurotransmitter signaling pathways might function in parallel to egl-6 by analyzing the egg-laying behavior of strains doubly mutant for egl-6 and genes required for the biosynthesis or storage of acetylcholine, dopamine, GABA, glutamate, octopamine, serotonin, or tyramine. We have found that egl-6, flp-10 and flp-17 deletion alleles enhance the egg-laying-constitutive phenotype of unc-17 and cha-1 mutants defective in acetylcholine signaling. We have further found that loss-of-function mutations affecting the egl-6 pathway suppress the egg-laying-defective phenotype of ace-2; ace-1 mutants, which have elevated levels of acetylcholine signaling as a consequence of decreased acetylcholinesterase activity.

Our observations suggest that FLP-10 and FLP-17 function together with a cholinergic signal to inhibit the egg-laying motor program. We are seeking the cholinergic circuits and acetylcholine receptors that function in parallel to EGL-6. We are continuing the characterization of the modulation of egg-laying by mutants defective in both acetylcholine signaling and signaling through EGL-6 and hope to learn under which circumstances these pathways are invoked to regulate C. elegans egg-laying behavior.

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