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

Niels Ringstad, Bob Horvitz
HHMI, Dept. Biology, MIT, Cambridge, MA 02139 USA

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.

Contact: ringstad@mit.edu
Lab: Horvitz