

Inhibition of *C. elegans* Egg-laying Behavior by Neuropeptide Signaling Pathways

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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 modulate *C. elegans* egg-laying behavior we are characterizing genes that when mutated cause severe egg-laying defects but do not strongly affect muscle function 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 it encodes a protein related to insect receptors for FMRFamide neuropeptides. Gene-dosage studies together with the molecular characterization of *egl-6* suggest that *egl-6* encodes a receptor for a signal that inhibits *C. elegans* egg-laying. A functional translational fusion of *egl-6* with GFP is expressed in egg-laying muscles and the HSN motoneurons, suggesting that *egl-6* acts in the egg-laying neuromusculature.

To identify ligands for EGL-6 we generated a panel of transgenic animals carrying extra copies of *C. elegans* genes predicted to encode neuropeptides. We identified four genes predicted to encode neuropeptides that, like *egl-6*, confer a strong egg-laying defect at high copy: *flp-10*, *flp-17*, *flp-22*, and *nlp-3*. The egg-laying defects conferred by increased dosage of *flp-10* and *flp-17* are strongly suppressed by a null allele of *egl-6*, suggesting that these genes encode ligands for the EGL-6 receptor. Furthermore, synthetic peptides corresponding to the predicted peptide products of the *flp-10* and *flp-17* loci can activate the EGL-6 receptor co-expressed in *Xenopus laevis* oocytes with G protein-gated inward rectifier K⁺ channels.

We have isolated mutants carrying deletions in the *flp-10*, *flp-17*, and *egl-6* genes. We are characterizing the modulation of egg-laying by these mutants and hope to learn under which circumstances this neuropeptide signaling pathway is invoked to regulate *C. elegans* egg-laying behavior.

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