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 motorneurons, 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.