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Determining the roles of octopamine and CREB in worm behavior

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To study processes that may underlie behavioral plasticity, we are analyzing the roles of the biogenic amine octopamine and the CREB protein in *C. elegans*.

Exogenous octopamine inhibits egg-laying, pharyngeal pumping and defecation. Octopamine has been identified in *C. elegans* extracts but has not been localized to specific cells. Octopamine biosynthesis requires a tyramine ß-hydroxylase (TBH) activity to convert tyramine to octopamine. We isolated a deletion of a putative *C. elegans* tyramine ß-hydroxylase gene (*tbh-1*) by screening a chemical deletion library. *tbh-1* mutants are viable and have no obvious abnormalities in brood size, egg-laying, chemotaxis, mechanosensation, thermotaxis or dauer formation. *tbh-1* mutants move more slowly than wild-type animals and are hypersensitive to exogenous serotonin in locomotion assays. Using immunohistochemistry we have shown that TBH-1 is localized to the cell bodies and neuronal processes of the two RIC interneurons, suggesting that the RIC neurons use octopamine as a neurotransmitter. We are further analyzing the role of octopamine and the RIC neurons in locomotion rate.

The cyclic AMP-response element binding protein CREB seems to play a central role in long-term memory in *Aplysia*, *Drosophila* and mice. We characterized a *C. elegans* CREB gene (*crb-1*). The similarity of CRB-1 to mammalian and *Drosophila* CREB family members is particularly striking in the predicted DNA-binding bZIP domain and cAMP-dependent kinase site. CRB-1 can bind to cyclic AMP-response element (CRE) sites *in vitro*. A *crb-1::GFP* transgene is ubiquitously expressed during early embryogenesis and is specifically expressed in several sensory neurons from the L1 stage to adulthood. We isolated a deletion allele of *crb-1* from a chemical deletion library. *crb-1* mutant animals are healthy and are being analyzed for behavioral defects.