Some *C. elegans* Ligand-gated Chloride Channels Are Receptors for Biogenic Amines

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Biogenic amines constitute a class of neuronal signaling molecules that function widely as neurotransmitters and neuromodulators in the vertebrate brain. The *C. elegans* nervous system expresses the biogenic amines serotonin, dopamine, tyramine and octopamine and uses them to modulate or coordinate simple motor programs. Most biogenic amine receptors are G protein-coupled receptors that function to regulate intracellular second-messenger systems. Recently, chloride channels that are directly activated by serotonin and by histamine have been identified in the *C. elegans* and arthropod nervous systems, respectively, indicating that ligand-gated chloride channels (LGCCs) might constitute a new class of receptor for biogenic amines.

We expressed 26 presumptive chloride channels encoded by the *C. elegans* genome in *Xenopus* oocytes and tested each for biogenic amine receptor activity. We identified three chloride channels that function as biogenic amine receptors in vitro: a dopamine receptor, a tyramine receptor and a low-affinity serotonin receptor. The expression patterns of reporter transgenes suggest that these receptors are expressed in distinct subsets of the *C. elegans* neuromusculature. We isolated mutants with deletions in the three genes that encode these amine receptors to test whether these receptors function in known biogenic amine signaling pathways. Mutants lacking the dopamine- and serotonin-gated chloride channels had grossly wild-type behavior. By contrast, mutants lacking the tyramine-gated chloride channel had defects in the control of foraging head movements but not in egg-laying behavior, indicating that this receptor mediates a subset of the known functions of tyramine in the control of *C. elegans* behavior. Our studies suggest that a general mode of action for biogenic amines in *C. elegans* is the direct control of membrane chloride conductances.

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