Identification and Characterization of *C. elegans* Amine-gated Chloride Channels

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Biogenic amines commonly function as neuromodulators by activating metabotropic G protein-coupled receptors. In vertebrates, the biogenic amine serotonin (5-HT) also functions as a fast-acting excitatory neurotransmitter by activating the ionotropic 5-HT_3 receptor, a non-selective cation channel. In *C. elegans*, 5-HT may function as a fast-acting inhibitory neurotransmitter through MOD-1, a 5-HT-gated chloride channel (Ranganathan, Cannon, and Horvitz, Nature 408: 470-475, 2000).

To determine whether there are other MOD-1-like receptors in *C. elegans*, we searched the *C. elegans* genome for sequences similar to the *mod-1* coding sequence and found 26 uncharacterized genes predicted to encode ligand-gated chloride channels. We are expressing each of these genes in *Xenopus* oocytes and testing them for amine receptor activity. So far we have identified three novel ionotropic receptors gated by biogenic amines. One of these receptors, encoded by the gene *T21F2.1*, is activated most potently by dopamine. Another, encoded by *Y113G7A.5*, is most potently activated by tyramine. A receptor encoded by the gene *T24D8.1* is activated by high concentrations of 5-HT and not by other tested amines. Ion-replacement studies suggest that, like MOD-1, these channels selectively pass chloride ions.

To understand how these receptors function *in vivo*, we have isolated deletion mutants in these three genes and are characterizing their behaviors. Mutants carrying a deletion in the gene *Y113G7A.5* have a Sho phenotype (Suppression of head oscillations-defective) suggesting that this ion channel functions in a tyraminergic signaling pathway *in vivo*. Mutants carrying a deletion in the gene *T21F2.1* have a defect in basal slowing, a dopamine-dependent modulation of locomotion, suggesting that this ion channel functions as a dopamine receptor *in vivo*. T21F2.1 and Y113G7A.5 are, to our knowledge, the first identified ionotropic receptors for tyramine and dopamine. Our studies and those of MOD-1 suggest a broad role for ligand-gated chloride channels in aminergic signaling in *C. elegans*.

Poster
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