

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

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Biogenic amines generally function as neuromodulators by activating metabotropic G protein-coupled receptors. In vertebrates, the biogenic amine serotonin (5-HT) also acts as a fast-acting excitatory neurotransmitter by activating the ionotropic 5-HT₃ 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, this approach has identified three novel ionotropic receptors gated by biogenic amines. One of these receptors is activated most potently by dopamine, another by tyramine, and one receptor is weakly activated by 5-HT and not by other known amines. Ion-replacement studies suggest that, like MOD-1, these channels selectively pass chloride ions. We are characterizing the pharmacological properties of these channels. We have found that some dopamine receptor antagonists, including chlorpromazine, haloperidol, spiperone, raclopride, and SCH₂₃₃₉₀ antagonize the current carried by the putative dopamine receptor. To understand how these receptors function *in vivo*, we have isolated deletion mutants in these three genes and are determining if any of these mutants are abnormal for any behaviors. The mutant with a deletion in the putative tyramine receptor gene has a phenotype consistent with behaviors known to be mediated by tyramine signaling (Alkema et al., IWM Abstract no. 14, 2003).