MOD-1 AND *MOD-5* CONTROL SEROTONERGIC NEUROTRANSMISSION AND EXPERIENCE-DEPENDENT MODULATION OF LOCOMOTORY BEHAVIOR

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Hermaphrodites respond to the presence of a bacterial lawn by slowing their rate of locomotion. Animals deprived of bacteria for 30 minutes exhibit enhanced slowing when they are reintroduced to a bacterial lawn. This modulatory response is mediated by serotonin. Mutations in *mod-1* and *mod-5* (modulation of locomotion defective) affect both the modulatory response and serotonergic neurotransmission.

mod-1 mutants display reduced slowing in the modulatory response and resistance to serotonin in assays of locomotion in liquid (exogenous serotonin inhibits the locomotion of wild-type animals). We cloned *mod-1* and performed electrophysiological studies using *Xenopus* oocytes to show that *mod-1* encodes an ion channel that is gated specifically by serotonin. *mod-5* mutants are defective in serotonin loading of the NSM neurons (C. Trent and B. Horvitz, unpublished observations), display more pronounced slowing than the wild type in the modulatory response, and are hypersensitive to exogenous serotonin in assays of locomotion in liquid. *mod-5* encodes a protein similar to mammalian serotonin reuptake transporters (SERTs), which are the proposed sites of action of the tricyclic antidepressants and the selective serotonin reuptake inhibitors (SSRIs), such as Prozac. We have confirmed that MOD-5 is a functional SERT by performing uptake assays using mammalian cells.

We did a non-clonal F2 screen for suppressors of *mod-5(n3314)* (a deletion allele) by seeking mutants no longer hypersensitive to serotonin. From a screen of 18,300 genomes we obtained 61 independent isolates suppressed for the serotonin hypersensitivity to varying degrees. Fifteen of these 61 isolates also suppress to varying degrees the Mod phenotype caused by *mod-5(n3314)*, i. e., after food-deprivation and re-introduction to bacteria, these isolates move faster than *mod-5(n3314)* mutants. We are mapping *n3461* and *n3488,* two suppressor mutations that strongly suppress both the serotonin hypersensitivity and the Mod phenotype.