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A *mod-5* SUPPRESSION SCREEN FOR GENES INVOLVED IN SEROTONERGIC NEUROTRANSMISSION

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Wild-type animals that have been food deprived slow their locomotory rate in response to bacteria (the enhanced slowing response). Food-deprived *mod-5(n3314)* mutants encountering bacteria slow even more than food-deprived wild-type animals, exhibiting a hyperenhanced slowing response. *mod-5* mutants were originally identified as defective in serotonin (5-HT) reuptake, and the *mod-5* gene has recently been shown to encode a 5-HT reuptake transporter. To identify additional genes involved in serotonergic neurotransmission, we designed a screen for suppressors of the *mod-5(n3314)* mutation. The screen took advantage of a second characteristic of *mod-5(n3314)* mutants: hypersensitivity to exogenous 5-HT. When placed in M9 containing 5-HT, *mod-5(n3314)* mutants stop swimming sooner than wild-type animals. Suppressors of *mod-5(n3314)* can be identified as animals that continue to swim after *mod-5(n3314)* mutants would have stopped.

We screened 18,350 haploid genomes and obtained 61 independent *mod-5* suppressors. Eighteen of these isolates were found also to suppress the hyperenhanced slowing response exhibited by *mod-5(n3314)* mutants. Interestingly, the strength of suppression of the hyperenhanced slowing response did not strictly correlate with the strength of suppression of hypersensitivity to exogenous 5-HT. This observation may indicate that the exogenous 5-HT and locomotion assays assess different pathways that involve 5-HT neurotransmission. To date, six suppressors have been mapped to linkage groups: one to LG I, three to LG II, one to LG V, and one to LG X. Further mapping experiments are underway to determine the identities of these genes.

Our suppressors may define genes that act downstream of the synapses at which *mod-5* acts, *i.e.*, genes involved in transducing the signal in postsynaptic neurons or muscle cells responsible for slowing the locomotory rate of the animal. We also expect to find genes acting upstream of these synapses, because a mutation in the gene *cat-4*, which is involved in 5-HT biosynthesis, suppresses the exogenous 5-HT hypersensitivity of *mod-5(n3314)* mutants.