

131. 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 upon encountering bacteria (the enhanced slowing response). *mod-5* mutants slow even more than wild-type animals (the hyperenhanced slowing response). *mod-5* mutants were originally identified as defective in serotonin (5-HT) reuptake, and the *mod-5* gene encodes a 5-HT reuptake transporter. To identify additional genes involved in 5-HT signaling, we designed a screen for suppressors of *mod-5*. The screen takes advantage of a second characteristic of *mod-5* mutants: hypersensitivity to exogenous 5-HT. When placed in M9 containing 5-HT, *mod-5* mutants become immobilized sooner than wild-type animals. Screening for animals that continue to move after *mod-5* mutants would have stopped allows us to identify suppressors of *mod-5*.

We previously screened 22,000 EMS-mutagenized haploid genomes and obtained 13 independent *mod-5(n3314)* suppressors. At least five of these suppressors also suppress the hyperenhanced slowing response exhibited by *mod-5(n3314)* mutants. All 13 mutants confer semidominant suppression of the 5-HT hypersensitivity of *mod-5(n3314)* animals. This semidominance and the variability of this suppression have made mapping difficult. We have employed two strategies to circumvent this problem. First, by further characterizing the phenotypes of *mod-5(n3314)* suppressors, we have identified other defects that they exhibit. If these defects are caused by the same mutation that suppresses the 5-HT hypersensitivity of *mod-5(n3314)*, then mapping experiments may be performed by following those defects. Second, we have begun a screen using the Mos1 transposon as a mutagen (Bessereau, J. L. et al, (2001) *Nature*, 413: 70-74). To date, ~8,000 haploid genomes have been screened and three suppressors identified. One suppressor is an allele of *mod-1*, which encodes a 5-HT-gated Cl⁻ channel. Mutations in *mod-1* were previously known to partially suppress *mod-5*. We will continue to screen Mos1-mutagenized animals to identify additional suppressors. We will also characterize the existing mutants and identify the genes disrupted by the Mos1 transposon.

The suppressors may define genes that act downstream of the synapses at which *mod-5* acts, *i.e.*, genes with products that are involved in transducing the signal in postsynaptic neurons or muscle cells responsible for slowing the locomotory rate of the animal. We will focus on genes that mediate the enhanced slowing response and hope to define both the molecular signals that elicit this behavior as well as the neural circuit(s) through which these signals act.