FOOD-DEPRIVATION AND MODULATION OF LOCOMOTORY BEHAVIOR: *MOD-6* AND A SCREEN FOR NEW GENES

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Upon entering a bacterial lawn, well-fed hermaphrodites exhibit a basal slowing response while acutely food-deprived worms exhibit enhanced slowing (see abstract by Ranganathan et al.). A number of cloned genes define a molecular pathway in which serotonin signaling is critical for this enhanced slowing response. Food-deprived worms are no more sensitive to exogenous serotonin than well-fed worms, suggesting that food-deprivation induces a physiological change that modulates serotonin release rather than alters the sensitivity to endogenous serotonin. *mod-6(n3076)* (modulation of locomotion defective) was isolated in a screen for mutants that failed to exhibit enhanced slowing after food-deprivation. Mutations in *mod-1,* which encodes an ionotropic serotonin receptor, and in *goa-1*, which encodes a G protein coupled to serotonin signaling, result in a Mod phenotype. These animals are resistant to immobilization by exogenous serotonin, indicating that they define components that act postsynaptically to serotonin. By contrast, *mod-6* animals are modulation defective, serotonin positive by immunostaining, sensitive to exogenous serotonin, and flouxetine (Prozac) resistant. These characteristics suggests that *mod-6* may be involved in modulating serotonin release in response to food-deprivation. We have mapped *mod-6* to a small interval on chromosome I and are presently attempting to clone the gene by cosmid rescue.

We are also performing a screen to isolate more mutants that fail to modulate their locomotory rate after food-deprivation. Specifically, we are looking for suppressors of *n3314,* a deletion allele of the *mod-5* serotonin re-uptake transporter. *mod-5(n3314)* sensitizes animals to endogenous serotonin release, resulting in immobilization of food-deprived animals upon re-entering a bacterial lawn. We hope to find mutations involved in detecting food-deprivation, storing this information, modulating the release of serotonin, and signaling downstream events directly involved in slowing. Our primary focus will be on new genes involved in changing the internal state of the animal in response to food-deprivation. These mutants would likely be modulation-defective and flouxetine-resistant but still sensitive to exogenous serotonin.