**Insulin and Neuropeptide Signaling Mutants Are Defective in the Enhanced Slowing Response Induced by Food Deprivation**

**Daniel Omura** and Bob Horvitz HHMI, Dept. Biology, MIT, Cambridge, MA 02139 USA

Well-fed animals encountering a bacterial lawn exhibit a dopamine-dependent "basal slowing response" that is completely suppressed in *cat-2(n4547)* deletion mutants, which lack dopamine. Acutely food-deprived animals exhibit an "enhanced slowing response" mediated in part by serotonin. The serotonin-gated chloride channel MOD-1 (modulation of locomotion defective) and the serotonin reuptake transporter MOD-5 are involved in propagating and attenuating the enhanced slowing response, respectively. Interestingly, a new *tph-1(n4622)* deletion mutant lacking serotonin exhibits some enhanced slowing, indicating that this behavior is dependent on yet unidentified factors.

To identify mutants that may perceive a perpetual state of food deprivation, we screened for mutants that exhibit constitutive enhanced slowing in a *mod-5(n3314)*-sensitized background. From this screen we isolated an allele of mrp-1 (multidrug resistance protein family). *mod-5(n3314); mrp-1(n4167)* mutants move well in the absence of bacteria and become paralyzed upon entering a bacterial lawn even when well fed. This paralysis is antagonized by a mutation in *mod-1*, suggesting that serotonin-dependent slowing is occurring in the well-fed state. Yabe et al. (2002 Japanese Worm Meeting) found that *mrp-1* is synthetically dauer-constitutive with *unc-31*, leading us to investigate the role of dauer genes in enhanced slowing. Thus far we have found that a mutants defective in the insulin receptor *daf-2* also exhibit constitutive enhanced slowing in a *mod-5(n3314)* background. We have also identified a role for neuropeptide signaling in the modulation of enhanced slowing: mutants defective in the neuropeptide receptor *npr-1(ky13)* or its ligand *flp-21(ok889)* have greatly reduced slowing in the food-deprived state.

To understand how *C. elegans* neuropeptide and insulin signaling pathways interface with food-deprivation to modulate locomotion, we are studying the well-fed and food-deprived responses of these mutants to food with respect to the normal dependence of basal slowing on dopamine and of enhanced slowing on serotonin. Both well-fed and food-deprived *npr-1* mutants exhibit slowing on food which is completely suppressed by *cat-2(n4547)*. Thus they seem to display basal instead of enhanced slowing. By contrast, well-fed *mod-5; daf-2* mutants exhibit slowing on food that is reduced in a *mod-1* mutant background and thus they always seem to exhibit some enhanced slowing. In a fashion analogous to mammalian energy metabolism, the *C. elegans* neuropeptide Y receptor homolog NPR-1 may signal a food-deprived state, while the insulin receptor DAF-2 may signal a well-fed state.