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A Novel Conserved Gene that Might Be Involved in Synaptic Vesicle Release. **Allan Froehlich**, Bob Horvitz. HHMI, Dept. Biology, MIT, Cambridge, MA 02139 USA.

To identify mutants that perceive a constitutive state of food deprivation, we screened for mutants that behave as if they had been food-deprived when well fed. Well-fed *C. elegans* that encounter a bacterial lawn slow their locomotion, exhibiting the basal-slowing response. Acutely food-deprived animals slow more upon entering a bacterial lawn, exhibiting the enhanced-slowing response. Using a *mod-5* deletion background, we screened for mutants that exhibited enhanced slowing in the well-fed state; deletion of *mod-5*, which encodes a serotonin reuptake transporter, provided a sensitized strain background facilitating the recovery of mutants. We isolated 17 mutants that were restored to normal locomotion on food by methiothepin, a serotonin-gated receptor antagonist, suggesting that the mutations affect serotonin signaling and the ability to modulate behavior in response to past feeding experience.

Two of the 17 mutants, *n4022* and *n3925*, failed to complement each other and mapped to a 50 kb region on LG III. We identified a single gene, *C44B9.1*, capable of rescuing the locomotion defects of *n4022*. We identified in the *n4022* and *n3925* strains single point mutations in *C44B9.1* predicted to result in premature stop codons. The protein encoded by *C44B9.1* has no conserved domains of known function but is significantly similar to uncharacterized proteins found in other organisms, including humans (29% identical, 49% similar). Expression of a *C44B9.1* cDNA using a pan-neuronal promoter (*unc-119*), but not a body-wall muscle promoter (*myo-3*), rescued the locomotion and Hid defects (see below) of *n4022* animals. Using a transcriptional *gfp* reporter driven by a *C44B9.1* promoter, we observed expression in several head neurons, the identities of which we have not yet confirmed.

The *n4022* strain has a decreased sensitivity to aldicarb, an acetylcholinesterase inhibitor, and an increased sensitivity to levamisole, an acetylcholine receptor agonist, suggesting that the *n4022* defect may act presynaptically. The drug-sensitivity profile of *n4022* is similar to that of strains mutant for any one of several conserved genes implicated in the regulation of vesicle exocytosis (*unc-64, unc-31, hid-1*, and *aex-3*). Similar to mutations in this group of genes, *n4022* also causes high-temperature (27°C) induced dauer (Hid) formation on its own and dauer formation at 25°C in combination with *unc-31(e928)* or *unc-64(e246)*.

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Functional analysis of *acl-10*, a novel acyltransferase in *C. elegans*. **Rieko Imae**[1], Takao Inoue[1,3], Naoko Hara[1], Keiko Gengyo-Ando[2,3], Shohei Mitani[2,3], Hiroyuki Arai[1,3]. 1) Graduate School of Pharmaceutical Sciences, University of Tokyo; 2) Department of Physiology, Tokyo Women's Medical University School of Medicine; 3) Crest, JST.

Alignment of amino acid sequences from phospholipids acyltransferases, such as glycerol-3-phosphate acyltransferase, acl-glycerol-3-phosphate acyltransferase and dihydroxyacetonephosphate acyltransferase, reveals four regions of strong homology that comprise a glycerolipid acyltransferase signature sequence. There are more than 10 genes containing the acyltransferase signature sequence in human genome, of which physiological functions and substrate specificities are largely unknown. We identified 14 genes containing the signature sequence from *C. elegans* genome sequences (*acl-1~14*), and generated mutants lacking these genes. Among the genes, *acl-10* shows ~40% identity with the corresponding mammalian gene, but until recently, its functions have not been elucidated. In this study, we analyzed the physiological function of *acl-10* using the mutants lacking this gene.

The *acl-10* deletion mutant, *acl-10 (tm1045)*, exhibited dumpy morphology and severely uncoordinated movement at adult stage. In addition, *acl-10 (tm1045)* displayed hypersensitivity to the acetylcholine receptor agonist levamisole, suggesting that the signaling pathway leading to muscle contraction is activated in the mutants. These defects were fully rescued by *acl-10* expression at L4 stage, indicating that *acl-10* is required for muscle function rater than muscle formation. To further elucidate how *acl-10* controls muscle contraction, we performed rescue experiments using tissue-specific promoters (*unc-119p, myo-3p, dpy-7p*). Interestingly, all these constructs could rescue the movement defects of *acl-10 (tm1045)*. The hypersensitivity to levamisole was also rescued by neuronal or epithelial expression of *acl-10*, indicating that *acl-10* functions in a cell nonautonomous manner. We are currently investigating the mechanism of *acl-10* function in muscle contraction.

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Modulation of serotonin neurotransmission by EGb 761 in *C.elegans*. **Marishka K. Brown**, Yuan Luo. Dept Pharmaceutical Sciences, Univ of Maryland-Baltimore, Baltimore, MD.

Serotonin (5-hydroxytryptamine; 5-HT) is a monoamine that modulates behaviors in both invertebrates and vertebrates. Drugs that alter 5-HT signaling are potent antidepressants and affect metabolic rates. Previously, we observed that the *Ginkgo biloba* extract EGb 761 modulates the expression of 5-HT2_A receptors in mouse N2A neuroblastoma cells expressing amyloid beta and it enhances adult neurogenesis in aged mice in a mouse model of Alzheimer's disease. The aim of this present study is to determine the mechanism of action of EGb 761 on 5-HT transmission. In *Caenorhabditis elegans*, the 5-HT regulates several different behaviors including: egg-laying, pharyngeal pumping and locomotion. It has been shown that 5-HT regulates movement through MOD-1, which is a 5-HT chlorine gated channel found in the postsynaptic receptors in the worms. When exogenous 5-HT is applied to wild type worms, this causes a decrease in locomotion. Mutant *mod-1* worms are resistant to levels of exogenous 5-HT. In this study, wild type and mutant *mod-1* worms were treated with EGb 761 in the presence or absence of known 5-HT receptor agonist and antagonist, *meta* chlorophenylpiperazine (mCPP) and mianserin, respectively. Our results show that wild type worms treated with EGb 761 demonstrate a similar resistance to exogenous 5-HT as the *mod-1* mutants. However, *mod-1* worms that were treated with EGb 761 are less resistant to exogenous 5-HT, suggesting that the effect of EGb 761 depends on the postsynaptic 5-HT receptors in the worms. The question of whether the modifying effects of EGb 761 on 5-HT receptors are direct or indirect is presently under investigation.