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Regulation of Dopamine Signaling in the Modulation of Locomotion. **Robert O'Hagan**, Bob Horvitz. HHMI, Dept. Biology, MIT, Cambridge, MA. 02139.

Although genes encoding dopamine receptors and proteins involved in dopamine biosynthesis, uptake, and vesicle loading are known, mechanisms that regulate dopaminergic signaling are not well understood. Genetic studies of a dopamine-modulated behavior might elucidate mechanisms that regulate dopaminergic signaling.

When well-fed hermaphrodites encounter a bacterial lawn, they slow their locomotion by approximately 30%. This behavior, called the basal slowing response, requires dopaminergic signaling: animals mutant in *cat-2*, which encodes the tyrosine hydroxylase needed for dopamine biosynthesis, are defective in basal slowing behavior. However, animals that have been food-deprived for 30 minutes slow their locomotion by about 70% upon entry into a bacterial lawn, a behavior called the enhanced slowing response. Dopamine plays only a minor role in the enhanced slowing response, suggesting that food-deprivation might suppress dopaminergic signaling and promote the use of other neurotransmitters to mediate locomotory slowing. In other words, dopamine signaling is prone to regulation by the recent history of feeding. We hope to understand how sensation of bacteria evokes dopamine release and how dopaminergic signaling is regulated by the experience of food deprivation.

Screens for altered basal slowing responses might identify novel genes involved in processes such as: sensory transduction; dopamine vesicle loading, priming, and fusion; and regulation of dopamine receptors or their downstream effectors. Screens for animals that lack basal slowing behavior are difficult because of the small magnitude of the response. Instead, we are screening for mutants that exhibit an increased basal slowing response. We mutagenized *cat-2* mutants carrying a *cat-2*-rescuing extrachromosomal array and looked for animals that slowed excessively. Because this array is inherited by a fraction of progeny, we can determine if the increased basal slowing of isolates depends on *cat-2* and thus on dopamine. We are characterizing several isolates with *cat-2*-dependent increased basal slowing responses.

In the future, we plan to use *in vivo* electrophysiological techniques to record from neurons in the dopaminergic circuit to observe mechanisms that regulate quantal content, vesicular release, and the abundance and activity of receptors. We also plan to compare the physiology of wild-type animals and mutant isolates from our screens.

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The Role of Serotonin in Fat Regulation. **Supriya Srinivasan**, Leila Sadegh, Kaveh Ashrafi. Department of Physiology, University of California, San Francisco, CA.

The neurotransmitter serotonin is an important sensor of metabolic status and food availability in many species. In *C. elegans*, the exogenous administration of serotonin has a profound, dose-dependent reduction in fat content and interestingly, a parallel increase in food intake. The pharmacological data are corroborated by genetic evidence from the *tph-1(mg280)*mutant which lacks the ability to make serotonin. Animals deficient in serotonin production have increased fat and reduced food intake.

To understand the relationship between the serotonergic regulation of feeding rate and fat content, we have used a combination of forward genetics, RNAi-mediated gene inactivation and pharmacology to identify molecular components that underlie these processes. Interestingly, we have identified genes that fall into 3 classes: i) those required for reduced fat content of serotonin-treated animals without affecting feeding rate, ii) those required for increased feeding rate of serotonin-treated animals without concomitant effects on fat accumulation and iii) genes that suppress both the fat content and the feeding rate of serotonin-treated animals.

Tissue localization experiments show that genes regulating fat content are expressed either in the nervous system or in the intestinal fat-storing cells, while genes regulating feeding rate are expressed predominantly in the nervous system of animals. We have also found that serotonin reduces fat content by regulating fatty acid oxidation pathways rather than fatty acid synthesis pathways. Together, these results suggest that serotonin coordinately modulates behavior and metabolism to regulate fat content. Currently, we are focused on deciphering molecular mechanisms that couple neuronal serotonergic signaling to intestinal fat oxidation pathways.

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Caenorhabditis sp. 4 and *C. remanei* males induce passivity in con-and heterospecific virgin females. **L. Rene Garcia**. Department of Biology, Texas A&M Univ, College Station, TX.

I found that males from the gonochoristic species *Caenorhabditis* sp. 4 (PB2801) and *Caenorhabditis remanei* (PB4641) induced behavioral passivity in con- and heterospecific virgin females during the spicule insertion step of mating. Males from the hermaphroditic species *Caenorhabditis briggsae* (AF16, VT847, PB826) also induced behavioral passivity in *Caenorhabditis* sp. 4 and *C. remanei* females, but not in their own conspecific hermaphrodites. *Caenorhabditis elegans* males (N2, CB4855, CB4856) did not induce mating-induced behavioral passivity in con- or heterospecific mates. I used *C. elegans* male spicule insertion behavior as a reference to understand how gonochoristic males induce behavioral changes in their mates. Through comparative laser ablation- and behavioral analyses between *C. elegans* and *C. remanei*, I found that gonochoristic males required the SPC neurons, the p.c.s. neurons and the somatic gonad to produce a soporific factor that immobilizes virgin females and stimulates their vulval slit to widen during copulation. *C. elegans* and *C. briggsae* hermaphrodites and non-virgin gonochoristic females were not affected by this factor. At present, I am using the *C. elegans* hermaphrodite anatomy and molecular biology as a reference to explore potential cells and molecules in gonochoristic females that respond to the male soporific factor. I found that the uterine vulval cells are required for gonochoristic females to be sedated by males. In *C. elegans*, the UV1 cells are believed to have secretory properties; thus I plan to over-express and RNAi-knock down *C. remanei* and species 4 genes that in *C. elegans* are expressed in the UV1 cells.