

Gap junctional communication in the intestine affects social feeding behavior via FLP-21 and the NPR-1 mediated signaling pathway

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Abstract

Communication between the gut and the nervous system coordinates aspects of behavior and responses to stressors. When actively feeding, *C. elegans* executes a digestive motor program triggered by a calcium wave that requires gap junctional connections along the intestinal length. Loss of function of the innexin-16 (*inx-16*) gap junctional subunit results in altered group feeding behavior, leading to social feeding characterized by increased body contact, or clumping, between animals. Using genetic analysis, our data shows that *inx-16* genetically interacts with *npr-1* and *flp-21*, but not *daf-7*. Thus, gut-to-brain signaling influences social versus solitary feeding behavioral choice.

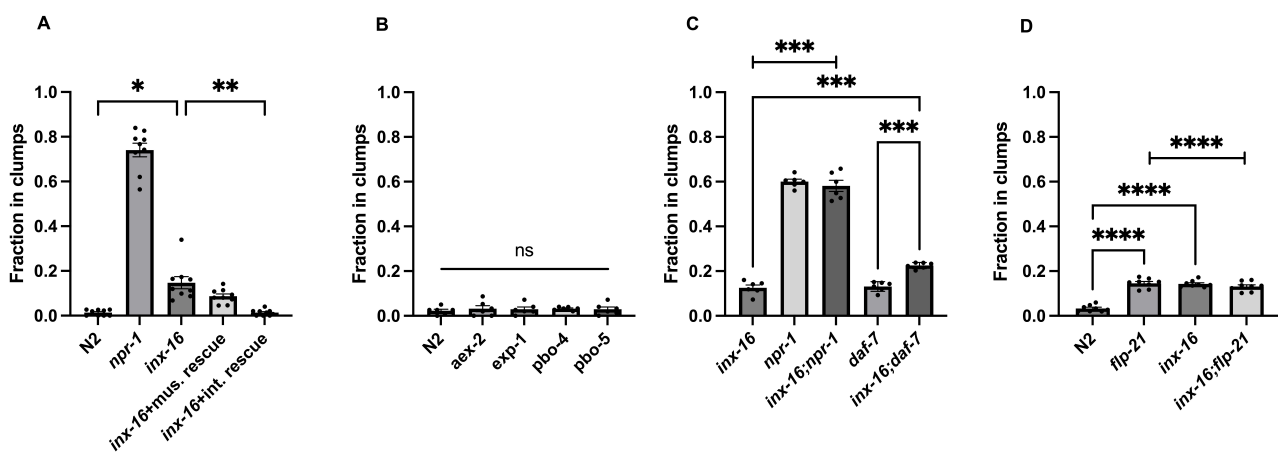


Figure 1. *inx-16* mutation results in enhanced aggregation and genetically interacts with both *npr-1* and *flp-21*:

Figure 1: *inx-16* loss of function increases aggregation, and genetic interaction assays show an interaction between *flp-21* and *npr-1* but not *daf-7*. (A) Aggregation fractions for *N2*; *npr-1(ad609)*; *inx-16(tm1589)* mutant with *inx-16* (+) expressed in the muscle (mus.) and *inx-16* mutant with *inx-16* (+) expressed in the adult intestinal (int.), both labeled as + “rescue”, n=9 for all strains. (B) Aggregation fractions for defecation mutants compared to *N2*, mutants used: *aex-2(sa3)*; *exp-1(sa6)*; *pbo-4(ok583)*; *pbo-5(ox4)*; n=6 for all strains. (C) Aggregation fractions for single and double mutants of the following genes: *inx-16(tm1589)*; *npr-1(ad609)*; *daf-7(e1372)*; n=6 for all strains. (D) Aggregation fractions for single and double mutants of the following genes: *flp-21(ok889)*; *inx-16(tm1589)* alongside *N2*; n=8 for all strains. Statistical significance: *p<0.05; **= p<0.01; ***<0.001; ****<0.0001; ns is not significant. Brackets used for comparisons between two mutants; line used across three strains for genetic interactions.

Description

Organisms adapt to their dynamic internal and external environments by leveraging systemic physiological responses using signaling pathways involving multiple tissues and extensive cross-talk. Recently, the gut has emerged as an important signaling center keenly attuned to an animal's feeding state, food quality, and pathogenic exposure. Within *C. elegans*, gut-derived secreted peptide signals influence feeding, stress response, waste release and avoidance behavior by acting on neurons of the enteric and central nervous systems (Artan et al., 2016; Jia et al., 2024; Sural et al., 2025). For example, *INS-7* and *INS-35* regulate the NSM neuron to adjust pharyngeal pumping rates (Sural et al., 2025). Additional insulin family members such as *INS-3* and *INS-11* function in gut-to-brain signaling pathways (Lee and Mylonakis, 2017; Veuthey et al., 2025). Several non-insulin peptides are also involved. *FLP-2* (FMRFamide-like peptide) acts via the interneuron AIY to induce responses to oxidative stress within the animal (Jia et al., 2024). *NLP-40* (Neuropeptide-like protein) is released to instruct the posterior enteric neurons, AVL and DVB, to elicit steps of the digestive/defecation motor program; its release is tied to a periodic calcium wave that occurs in well-fed animals with a regular frequency of 45-55 seconds (Choi et al., 2023; Mahoney et al., 2008; Wang et al., 2013).

This regular calcium wave may trigger release of additional peptides that influence nervous system behavior more broadly. Several mutants with poor digestive waste release originally identified due to their constipated phenotypes turn out to encode integral components of peptide processing and release such as [egl-3](#), [egl-21](#), [aex-1](#), [aex-4](#), and [aex-5](#) (Husson et al., 2007; Khawand et al., 2026; Mahoney et al., 2008). At least one peptide, [NLP-40](#), is released in time with the digestive motor program, via activation of synaptotagmin-2 ([snt-2](#)), a calcium-sensing protein that triggers DCV fusion (Wang et al., 2013). The tyramine response pathway offers additional evidence of calcium-triggered peptide release (Veuthey et al., 2025). This enticing evidence suggests that the rhythmic calcium flux that triggers [NLP-40](#) release, and other steps of the digestive/defecation motor program, may be used more broadly to influence behavioral choices where feeding and nutritional status are relevant. With this notion in mind, we explored an observation of social feeding behavior in a mutant that alters intestinal calcium wave dynamics.

The [innexin-16](#) ([inx-16](#)) gap junction subunit is critical for periodic intestinal calcium waves associated with the digestive motor program; loss of function [inx-16](#) mutants disrupt the intestinal calcium wave and greatly reduce the digestive motor program steps that require [NLP-40](#) release (Peters et al., 2007). During routine maintenance of [inx-16\(tm1589\)](#), we observed increased aggregation of well-fed worms and became intrigued. To explore this further, we assayed for social feeding behavior quantitatively. For comparison, we included [N2](#), a solitary strain, and a social feeding strain, [npr-1\(ad609\)](#). The gene, [npr-1](#), encodes a *C. elegans* receptor related to neuropeptide Y and is neuronally expressed. When active, [NPR-1](#) inhibits the tendency of animals to aggregate in groups, suppresses oxygen level preferences, and affects bordering (de Bono and Bargmann, 1998; Gray et al., 2004). The [npr-1](#) allele we used, [ad609](#), has been characterized to be a strong loss of function allele, equivalent to a genetic null (de Bono and Bargmann, 1998). Our results show that [inx-16](#) mutant animals maintain contact with other animals more frequently than wild-type ([N2](#)) solitary worms; young adult [inx-16\(tm1589\)](#) animals demonstrated a significant difference in the number of [inx-16](#) animals found in direct contact with their peers compared to [N2](#) (~0% vs. ~15%; Figure 1A). Yet, the [inx-16](#) phenotype is much weaker than the [npr-1\(ad609\)](#) allele (~80% vs. ~15%; Figure 1A).

To verify that [INX-16](#) functions within the intestine to cause the observed tendency to aggregate, we employed tissue specific rescue of [inx-16](#) mutants. Our and others' [inx-16](#) expression analyses indicated that [inx-16](#) was only expressed in the intestine, yet two studies have provided phenotypic evidence suggesting additional areas of function (Bhattacharya et al., 2019; Liu et al., 2013; Sojka et al., 2025). Intestine-specific rescue was achieved using a construct with a short, well-defined fragment, regulatory sequence of the egg yolk protein, vitellogenin-2, ([vit-2](#)) gene, placed upstream of an [INX-16](#) translational fusion (MacMorris et al., 1992). Prior work using this construct led to full rescue of the defecation defects in adults (Peters et al., 2007). Likewise, solitary feeding behavior was restored in the [inx-16+pvit-2](#) intestinal rescue line (Figure 1A). By contrast, driving expression of [inx-16](#) in body wall muscles, using the [myo-3](#) promoter, was unable to restore solitary (wild-type) feeding behavior (Figure 1A; Liu et al., 2013). These data suggest that intestinal [INX-16](#) function contributes to the animal's feeding behaviors.

Having shown that [inx-16](#)'s actions in the intestine can rescue the social feeding phenotype, we queried whether aggregated feeding was a common feature of mutants with impaired digestive waste release (Thomas, 1990). Defecation mutants induce constipation. One constipated mutant with defects in the expulsion step, [exp-1](#), disrupts an excitatory GABA-ergic receptor in enteric muscles and has been shown to mildly increase social feeding behavior (Beg and Jorgensen, 2003; Bendesky et al., 2012). We assayed this mutant, and others, selecting a set of mutants that affect each defecation motor step and all tissue types involved in the motor program (Branicky and Hekimi, 2006; Thomas, 1990). Two genes required for the first motor step (the posterior body contraction), the intestinal sodium proton exchanger, [pbo-4/nhx-7](#), and the downstream proton-gated ion channel, [pbo-5](#), localized to body wall muscles, were tested (Beg et al., 2008; Pfeiffer et al., 2008). Neither of these Pbo mutants showed increases in social feeding in comparison to [N2](#) (Figure 1B). The later steps of the program, anterior body contraction and enteric muscle contraction, require [NLP-40](#) release from the intestine to stimulate GABA release from enteric neurons, AVL and DVB (Wang et al., 2013). [NLP-40](#) binding activates [AEX-2](#), a g-protein coupled receptor, on these neurons (Allman et al., 2016; Mahoney et al., 2008). Like the Pbo mutants, [aex-2\(sa3\)](#) showed no significant increase over wild-type in our aggregation assay (Figure 1B). In our assays, [exp-1\(sa6\)](#) did not increase aggregation, which differs from prior findings that reported a small but significant increase (Bendesky et al., 2012). Though our defecation mutant panel is not exhaustive, these data suggest that the social feeding phenotype of [inx-16](#) is not broadly shared with mutants suffering from constipation; disrupting defecation per se does not alter social feeding behavior in *C. elegans*.

Two key gene pathways control the choice between solitary and social feeding behavior: [npr-1](#) and [daf-7](#). Therefore, we used genetic assays to elucidate potential connections between [inx-16](#) and these known pathways (de Bono and Bargmann, 1998; de Bono et al., 2002). Double mutants of [inx-16](#) with [daf-7\(e1372\)](#) and [npr-1\(ad609\)](#) were constructed and tested alongside single mutants to determine whether the double mutant lines had enhanced aggregation. The combination of [inx-16](#) and [daf-7\(e1372\)](#) enhanced aggregation substantially, with the [inx-16;daf-7](#) double mutant exhibiting increased aggregation compared to the [daf-7](#) mutant alone, approximately 23% for the double compared to ~13% for either single mutants (Figure 1C). This additive effect is consistent with [inx-16](#) functioning at least partly independently of [daf-7](#). By contrast, the combination of [inx-16](#) and the strong loss of function [npr-1](#) allele, [ad609](#), did not augment the social feeding

level relative to that of *npr-1* alone. The *inx-16;npr-1* double mutants exhibit no increase in aggregation compared to the *npr-1* mutant alone (60% for the double compared to 58% for the single mutant, Figure 1C). The results of a two-way ANOVA analysis support a highly significant genetic interaction between *inx-16* and *npr-1* ($P < 0.003$; $F = (1, 20) = 19$). These findings are consistent with *inx-16* functioning via the *npr-1* pathway to mediate social feeding behavior.

Since our findings placed *inx-16* within the *npr-1* pathway rather than the *daf-7* pathway, we searched for *NPR-1* ligands with evidence of intestinal expression. Of the two identified *NPR-1* ligands, *FLP-18* and *FLP-21*, *flp-21* showed intestinal expression in addition to a subset of neurons (Kubiak et al., 2003; Rogers et al., 2003). The *flp-21* mutation causes a significantly increased propensity for animals to aggregate, enhancing aggregation to ~15% (Figure 1D). Interestingly, *flp-21*'s magnitude of impact on feeding behavior is similar to that of *inx-16* mutation, ~15% for *flp-21* vs. ~14% for *inx-16* (Figure 1D; Rogers et al., 2003). Thus, we hypothesized that *FLP-21* could be released from the intestine following calcium waves in a manner analogous to *NLP-40* release. To begin to investigate this model, we explored epistasis between *inx-16* and *flp-21*. The double mutant line exhibited an aggregation profile very similar to that of either individual mutant strain (*inx-16;flp-21* = ~ 13%; Figure 1D). Statistical analysis for gene interaction upholds this epistatic relationship ($P < 0.0001$; $F = (1, 28) = 89$). Our results support a model placing *FLP-21* release downstream of *INX-16* function, and by inference the rhythmic intestinal calcium wave that directs the digestive motor program (Dal Santo et al., 1999; Espelt et al., 2005; Teramoto and Iwasaki, 2006).

Due to *flp-21*'s reported intestinal localization, we suggest that *inx-16*'s social feeding phenotype may be due to reduced *FLP-21* release from the intestine. Since *NPR-1* signaling dampens social feeding, loss of *FLP-21* would increase aggregation, as seen in both *inx-16* and *flp-21* mutants. Our model is supported by the previously reported epistasis analysis of *flp-21(pk1601)* and *npr-1(ad609)*; this *flp-21* allele did not enhance *npr-1(ad609)*'s social feeding level, matching our results (Figure 1C; Rogers et al., 2003). Given that *flp-18*, the other known *NPR-1* ligand, is not expressed in the intestine, *flp-18* presumably remains active in the *inx-16* mutant, allowing ample residual suppression of social feeding to result in the modest aggregation seen in both the *inx-16* and *flp-21* mutants (Figure 1D; Kapahi et al., 2010).

In summary, our findings demonstrate a behavioral feeding phenotype associated with disrupted intestinal calcium wave dynamics. We propose that this phenotype is due to disruption of *FLP-21* mediated activation of *NPR-1*. Moreover, the social feeding phenotype of *inx-16* suggests that the periodic intestinal calcium waves serve to regulate peptide release broadly, influencing a host of behaviors beyond defecation and adding to the growing body of evidence illustrating the importance of gut-to-brain signaling for animal behavior.

Methods

Strain maintenance and construction

C. elegans strains were cultured on standard NGM plates seeded with *OP50* bacteria using standard protocols. Double *daf-7* and *npr-1* mutant strains were generated using standard genetic crossing, selection based on dauer or aggregation phenotype, followed by sequencing to confirm genotypes. For *flp-21*, the large deletion allowed the use of PCR tracking prior to sequencing.

Social feeding assay

Young adult animals were assayed blindly using a protocol adapted from De Bono and Bargmann (1998). Strains containing the *daf-7(e1372)* mutation were reared at 15°C to prevent dauer formation. NGM plates were seeded with 200 mL of *OP50* in a circular lawn about 25 mm in diameter. Approximately 150 well-fed day 1 adult worms were added and left at 20-22°C for 2 hours. Then, the fraction of animals in contact with two or more other animals along at least 50% of their body length was tallied by visual inspection. For each panel's experiments, the full set of strains was tested each assay day and the full set of assays were completed in a short time period.

Statistical analysis and graphing

For statistical analysis, Graphpad/Prism (Version 11 for macOS) was used. Each panel's data set was tested for Gaussian distribution. Only one panel's data set (A) showed some non-Gaussian distribution, so Kruskal-Wallis program was applied. Otherwise, ANOVA analysis followed by multiple comparisons using Tukey's test (one-way ANOVA for panels A and B; two-way ANOVA for panels C and D) was used. Statistical deviation was considered significant if $p < 0.05$. Bar graphs show all data points, mean and standard error of the mean. p value scores are listed for informative comparisons relevant to our study. Differences between *npr-1* and *N2*, or other mutants that were previously published and/or strikingly obvious were not specifically noted. For example, statistical tests between *N2* and *npr-1*; *inx-16* and *npr-1*; *npr-1* and *daf-7* were not highlighted to simplify the figures.

Reagents

Strain	Genotype	Available from

N2	Bristol isolate	CGC
EG3528	inx-16(tm1589) I	National BioResource Project (NBRP)
TA145	inx-16(tm1589) I; <i>oxEx559</i> (<i>pvit-2:INX-16::GFP</i>)	
CB1372	daf-7(e1372) III	CGC
DA609	npr-1(ad609) X	CGC
RB982	flp-21(ok889) V	CGC
RB793	pbo-4(ok583) X	CGC
EG4	pbo-5(ox4) V	CGC
JT3	aex-2(sa3) X	CGC
JT6	exp-1(sa6) II	CGC
TA149	inx-16(tm1589) I; npr-1(ad609) X	
TA155	inx-16(tm1589) I; daf-7(e1372) III	
TA156	inx-16(tm1589) I; flp-21(ok889) V	
ZW701	inx-16(tm1589) I; <i>zwEx701</i> [<i>pmyo-3::inx-16(+):GFP</i> + <i>pmyo-3::GFP</i>]	Zhao-Wen Wang Lab

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References

- Allman E, Wang Q, Walker RL, Austen M, Peters MA, Nehrke K. 2016. Calcineurin homologous proteins regulate the membrane localization and activity of sodium/proton exchangers in *C. elegans*. *American Journal of Physiology-Cell Physiology* 310: C233-C242. DOI: [10.1152/ajpcell.00291.2015](https://doi.org/10.1152/ajpcell.00291.2015)
- Artan M, Jeong DE, Lee D, Kim YI, Son HG, Husain Z, et al., Lee. 2016. Food-derived sensory cues modulate longevity via distinct neuroendocrine insulin-like peptides. *Genes & Development* 30: 1047-1057. DOI: [10.1101/gad.279448.116](https://doi.org/10.1101/gad.279448.116)
- Beg AA, Ernstrom GG, Nix P, Davis MW, Jorgensen EM. 2008. Protons Act as a Transmitter for Muscle Contraction in *C. elegans*. *Cell* 132: 149-160. DOI: [10.1016/j.cell.2007.10.058](https://doi.org/10.1016/j.cell.2007.10.058)
- Beg AA, Jorgensen EM. 2003. EXP-1 is an excitatory GABA-gated cation channel. *Nature Neuroscience* 6: 1145-1152. DOI: [10.1038/nm1136](https://doi.org/10.1038/nm1136)
- Bendesky A, Pitts J, Rockman MV, Chen WC, Tan MW, Kruglyak L, Bargmann CI. 2012. Long-Range Regulatory Polymorphisms Affecting a GABA Receptor Constitute a Quantitative Trait Locus (QTL) for Social Behavior in *Caenorhabditis elegans*. *PLoS Genetics* 8: e1003157. DOI: [10.1371/journal.pgen.1003157](https://doi.org/10.1371/journal.pgen.1003157)
- Bhattacharya A, Aghayeva U, Berghoff EG, Hobert O. 2019. Plasticity of the Electrical Connectome of *C. elegans*. *Cell* 176: 1174-1189.e16. DOI: [10.1016/j.cell.2018.12.024](https://doi.org/10.1016/j.cell.2018.12.024)
- Branicky R, Hekimi S. 2006. What keeps *C. elegans* regular: the genetics of defecation. *Trends in Genetics* 22: 571-579. DOI: [10.1016/j.tig.2006.08.006](https://doi.org/10.1016/j.tig.2006.08.006)

- Choi U, Hu M, Zhang Q, Sieburth D. 2023. The head mesodermal cell couples FMRFamide neuropeptide signaling with rhythmic muscle contraction in *C. elegans*. *Nature Communications* **14**, 4218 (2023). DOI: [10.1038/s41467-023-39955-8](https://doi.org/10.1038/s41467-023-39955-8)
- Dal Santo P, Logan MA, Chisholm AD, Jorgensen EM. 1999. The Inositol Trisphosphate Receptor Regulates a 50-Second Behavioral Rhythm in *C. elegans*. *Cell* **98**: 757-767. DOI: [10.1016/s0092-8674\(00\)81510-x](https://doi.org/10.1016/s0092-8674(00)81510-x)
- de Bono M, Bargmann CI. 1998. Natural Variation in a Neuropeptide Y Receptor Homolog Modifies Social Behavior and Food Response in *C. elegans*. *Cell* **94**: 679-689. PubMed ID: [9741632](https://pubmed.ncbi.nlm.nih.gov/9741632/)
- de Bono M, Tobin DM, Davis MW, Avery L, Bargmann CI. 2002. Social feeding in *Caenorhabditis elegans* is induced by neurons that detect aversive stimuli. *Nature* **419**: 899-903. DOI: [10.1038/nature01169](https://doi.org/10.1038/nature01169)
- Espelt MV, Estevez AY, Yin X, Strange K. 2005. Oscillatory Ca²⁺ Signaling in the Isolated *Caenorhabditis elegans* Intestine. *The Journal of General Physiology* **126**: 379-392. DOI: [10.1085/jgp.200509355](https://doi.org/10.1085/jgp.200509355)
- Gray JM, Karow DS, Lu H, Chang AJ, Chang JS, Ellis RE, Marletta MA, Bargmann CI. 2004. Oxygen sensation and social feeding mediated by a *C. elegans* guanylate cyclase homologue. *Nature* **430**: 317-322. DOI: [10.1038/nature02714](https://doi.org/10.1038/nature02714)
- Husson SJ, Janssen T, Baggerman G, Bogert B, Kahn-Kirby AH, Ashrafi K, Schoofs L. 2007. Impaired processing of FLP and NLP peptides in carboxypeptidase E (EGL-21)-deficient *Caenorhabditis elegans* as analyzed by mass spectrometry. *Journal of Neurochemistry* **102**: 246-260. DOI: [10.1111/j.1471-4159.2007.04474.x](https://doi.org/10.1111/j.1471-4159.2007.04474.x)
- Jia Q, Young D, Zhang Q, Sieburth D. 2024. Endogenous hydrogen peroxide positively regulates secretion of a gut-derived peptide in neuroendocrine potentiation of the oxidative stress response in *Caenorhabditis elegans*. *eLife* **13**: 10.7554/eLife.97503. DOI: [10.7554/eLife.97503](https://doi.org/10.7554/eLife.97503)
- Kapahi P, Chen D, Rogers AN, Katewa SD, Li PWL, Thomas EL, Kockel L. 2010. With TOR, Less Is More: A Key Role for the Conserved Nutrient-Sensing TOR Pathway in Aging. *Cell Metabolism* **11**: 453-465. DOI: [10.1016/j.cmet.2010.05.001](https://doi.org/10.1016/j.cmet.2010.05.001)
- Khawand DC, Clippinger AK, Ailion M. 2026. CPD-1 can compensate for EGL-21 to process neuropeptides. *MicroPubl Biol* **2026**: 10.17912/micropub.biology.001965. PubMed ID: [41573665](https://pubmed.ncbi.nlm.nih.gov/41573665/)
- Kubiak TM, Larsen MJ, Nulf SC, Zantello MR, Burton KJ, Bowman JW, Modric T, Lowery DE. 2003. Differential Activation of “Social” and “Solitary” Variants of the *Caenorhabditis elegans* G Protein-coupled Receptor NPR-1 by Its Cognate Ligand AF9. *Journal of Biological Chemistry* **278**: 33724-33729. DOI: [10.1074/jbc.M304861200](https://doi.org/10.1074/jbc.M304861200)
- Lee K, Mylonakis E. 2017. An Intestine-Derived Neuropeptide Controls Avoidance Behavior in *Caenorhabditis elegans*. *Cell Reports* **20**: 2501-2512. DOI: [10.1016/j.celrep.2017.08.053](https://doi.org/10.1016/j.celrep.2017.08.053)
- Liu P, Chen B, Altun ZF, Gross MJ, Shan A, Schuman B, Hall DH, Wang ZW. 2013. Six Innexins Contribute to Electrical Coupling of *C. elegans* Body-Wall Muscle. *PLoS ONE* **8**: e76877. DOI: [10.1371/journal.pone.0076877](https://doi.org/10.1371/journal.pone.0076877)
- MacMorris, M., Broverman, S., Greenspoon, S., Lea, K., Madej, C., Blumenthal, T. & Spieth, J. Regulation of vitellogenin gene expression in transgenic *Caenorhabditis elegans*: short sequences required for activation of the *vit-2* promoter. *Mol Cell Biol* **12**, 1652–1662 (1992). DOI: [10.1128/mcb.12.4.1652-1662.1992](https://doi.org/10.1128/mcb.12.4.1652-1662.1992)
- Mahoney TR, Luo S, Round EK, Brauner M, Gottschalk A, Thomas JH, Nonet ML. 2008. Intestinal signaling to GABAergic neurons regulates a rhythmic behavior in *Caenorhabditis elegans*. *Proceedings of the National Academy of Sciences* **105**: 16350-16355. DOI: [10.1073/pnas.0803617105](https://doi.org/10.1073/pnas.0803617105)
- Peters MA, Teramoto T, White JQ, Iwasaki K, Jorgensen EM. 2007. A Calcium Wave Mediated by Gap Junctions Coordinates a Rhythmic Behavior in *C. elegans*. *Current Biology* **17**: 1601-1608. DOI: [10.1016/j.cub.2007.08.031](https://doi.org/10.1016/j.cub.2007.08.031)
- Rogers C, Reale V, Kim K, Chatwin H, Li C, Evans P, de Bono M. 2003. Inhibition of *Caenorhabditis elegans* social feeding by FMRFamide-related peptide activation of NPR-1. *Nature Neuroscience* **6**: 1178-1185. DOI: [10.1038/nn1140](https://doi.org/10.1038/nn1140)
- Sojka SE, Ezak MJ, Polk EA, Bischer AP, Neyland KE, Wojtovich AP, Ferkey DM. 2025. An Extensive Gap Junction Neural Network Modulates *Caenorhabditis elegans* Aversive Behavior. *Genes* **16**: 260. DOI: [10.3390/genes16030260](https://doi.org/10.3390/genes16030260)
- Sural S, Walker Z, Hobert O. 2025. Gut epithelium modifies enteric behaviors during nutritional adversity via distinct peptidergic signaling axes. *Science Advances* **11**: 10.1126/sciadv.adw1270. DOI: [10.1126/sciadv.adw1270](https://doi.org/10.1126/sciadv.adw1270)
- Teramoto T, Iwasaki K. 2006. Intestinal calcium waves coordinate a behavioral motor program in *C. elegans*. *Cell Calcium* **40**: 319-327. DOI: [10.1016/j.ceca.2006.04.009](https://doi.org/10.1016/j.ceca.2006.04.009)
- Thomas JH. 1990. Genetic analysis of defecation in *Caenorhabditis elegans*. *Genetics* **124**: 855-872. DOI: [10.1093/genetics/124.4.855](https://doi.org/10.1093/genetics/124.4.855)
- Veuthey T, Florman JT, Giunti Sn, Romussi S, De Rosa MaJ, Alkema MJ, Rayes D. 2025. The neurohormone tyramine stimulates the secretion of an insulin-like peptide from the *Caenorhabditis elegans* intestine to modulate the systemic stress response. *PLOS Biology* **23**: e3002997. DOI: [10.1371/journal.pbio.3002997](https://doi.org/10.1371/journal.pbio.3002997)

Wang H, Girskis K, Janssen T, Chan JP, Dasgupta K, Knowles JA, Schoofs L, Sieburth D. 2013. Neuropeptide Secreted from a Pacemaker Activates Neurons to Control a Rhythmic Behavior. *Current Biology* 23: 746-754. DOI: [10.1016/j.cub.2013.03.049](https://doi.org/10.1016/j.cub.2013.03.049)

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