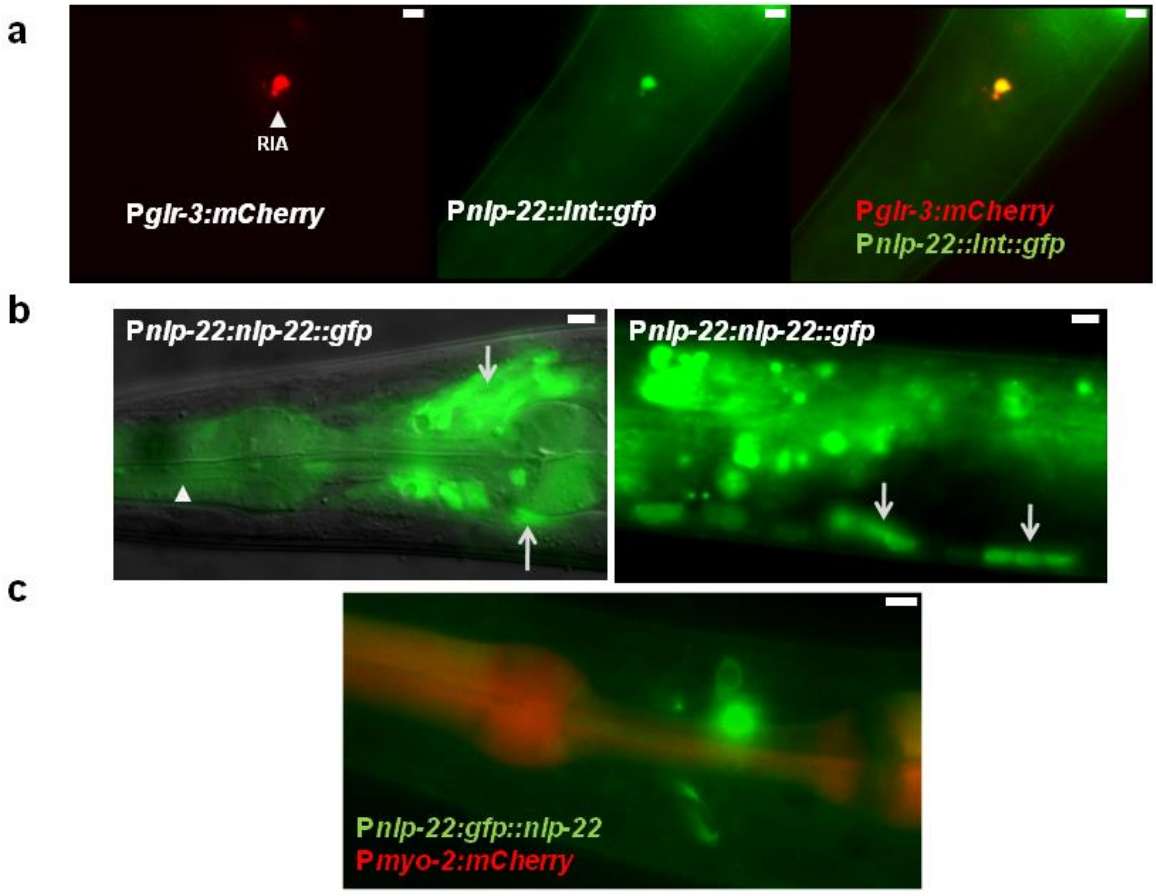
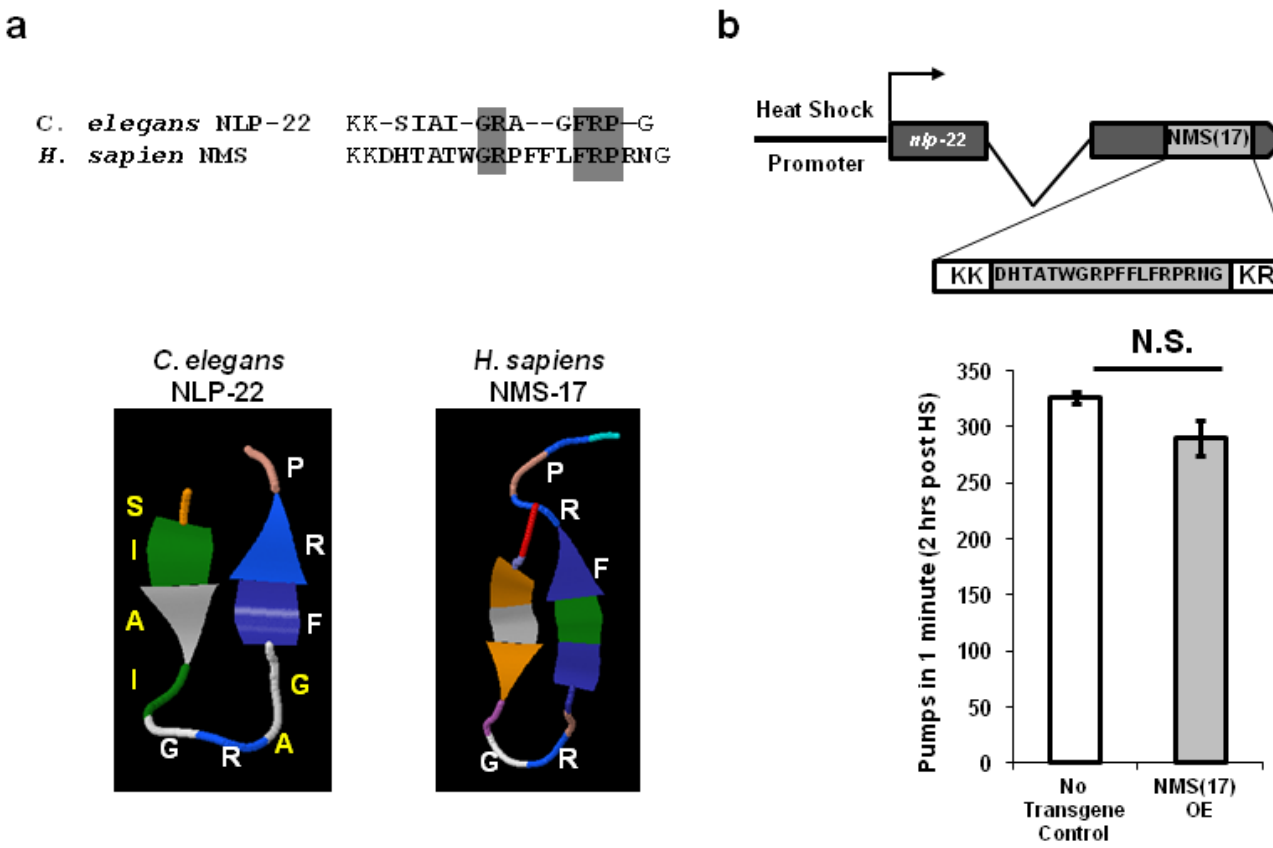


SUPPLEMENTARY FIGURE S1: *nlp-22* is expressed in the RIA interneurons and is secreted. (**a**) An animal expressing both the RIA specific reporter P*glr-3:mCherry* (red) and P*nlp-22:gfp* (green) shows co-localization in the RIA neurons (yellow). Only one of the pair of the RIA neurons is shown in this focal plane. (**b**) A Translational reporter in which *gfp* coding sequence replaces the *nlp-22* stop codon shows GFP spread to other neurons in the head (arrows, left panel), and in the ventral nerve cord (arrows, right panel). Anterior is to the left. Bright mCherry fluorescence in the pharynx, which was used as a marker for transgenesis, shows a signal in the gfp channel (arrow head). (**c**) A translational reporter in which *gfp* coding sequence was placed at the N-terminus of the NLP protein prior to the signal sequence shows GFP concentrated at the perimeter of the RIA neurons, suggesting that the GFP is interfering with secretion, and now marks the RIA plasma membranes. The transgenic animal is also marked with a red pharynx. Scale Bars = 5µM.



SUPPLEMENTARY FIGURE S2: Over-expression of Neuromedin S (17-33) does not induce behavioral quiescence. a) NLP-22 and human NMS-17, which consists of the last 17 amino acids of the full length NMS, are similar at the primary amino acid (top) and structural (bottom) levels. The conserved GR dipeptide and FRP tripeptide motifs are shown in white. b) Over-expression of NMS-17 in the context of the *C. elegans nlp-22* preproprotein using an inducible heat-shock promoter does not result in an inhibition of pharyngeal pumping (Student's two-tailed *t*-Test; Error bars represent s.e.m, N≥20).

Strain	Genotype	Array	Pumps per 20 Sec	N
N2	WT	-	88.4 ± 5.8	20
TJ375	WT	***gpIs1***[P*hsp-16.2:gfp*]	91.3 ± 5.84	20
NQ216	*unc-119*(*ed3*)	***qnEx95***[P*hsp-16.2:nlp-22*,P*myo-2:mCherry, unc-119*(+)]	8.4 ± 10.77	40
NQ251	WT	***qnIs142***[P*hsp-16.2:nlp-22*;P*hsp-16.2:gfp;* P*myo-2:mCherry; unc-119*(+)]	6.2 ± 10.38	37
NQ670	WT	***qnEx95***[P*hsp-16.2:nlp-22*;P*myo-2:mCherry; unc-119*(+)]	12.8 ± 19.0	20
DA509	*unc-31*(*e928*)IV	-	54.1 ± 5.4	15
NQ256	*unc-31*(*e928*)IV	***qnEx95***	1.8 ± 4.9*	25
KP1873	*egl-3*(*nu349*)V	-	41.3 ± 24.9	32
NQ319	*egl-3*(*nu349*)V	***qnEx95***	8.5 ± 11.3*	24
KP2018	*egl-21*(*n476*)IV	-	58.6 ± 18.0	18
NQ320	*egl-21*(*n476*)IV	***qnEx95***	4.4 ± 5.8*	36
MT1074	*egl-4*(*n479*)IV	-	71.0 ± 8.5	23
NQ321	*egl-4*(*n479*)IV	***qnEx95***	12.9 ± 14.0*	32
NQ668	*egl-4*(*n479*)IV	***qnIs142***	14.2 ± 10.2*	30
IB16	*ceh-17*(np1)I	-	62.1 ± 6.4	10
NQ230	*ceh-17*(np1)I	***qnEx95***	6.6 ± 9.8*	10
KG532	*kin-2*(*ce179*)X	-	101.2 ± 13.6	15
NQ605	*kin-2*(*ce179*)X	***qnIs142***	45.1 ± 23.1*	25
NQ667	*kin-2*(*ce179*)X	***qnEx95***	24.8 ± 12.8*	20
RB1288	*nmur-1*(*ok1387*)X	**-**	73.1 ±10.8	10
NQ274	*nmur-1*(*ok1387*)X	***qnEx95***	13.2 ± 12.9*	10
RB2526	*nmur-2*(*ok3502*)II	**-**	58.1 ± 21.3	10
NQ285	*nmur-2*(*ok3502*)II	***qnEx95***	13.6 ± 19.5*	20
VC1974	*nmur-3*(*ok2295*)X	**-**	70.3 ± 6.6	10
NQ275	*nmur-3*(*ok2295*)X	***qnEx95***	4.4 ± 5.4*	10
RB1284	*nmur-4*(*ok1381*)I	**-**	76 ± 3.3	7
NQ235	*nmur-4*(*ok1381*)I	***qnEx95***	3.1 ± 6.5*	7

Supplementary Table S1: *nlp-22* over-expression analyses. *nlp-22* over-expression reduces pharyngeal pumping rates in all genetic backgrounds tested, including those previously implicated in regulating quiescence and those implicated in processing some neuropeptides. Shown are the average pumping rates with standard deviations. *P<.005, 2-tailed Wilcoxon Rank Sum test, comparing the mutant over-expressing *nlp-22* to mutant alone.

Strain	Genotype	Transgene Array	Total Quiescence (min)	Peak Fraction Quiescence	L4 lethargus Duration (min)	End of L3L to Start of L4L (hr)	N
N2	WT	-	91.3 ± 7.5	0.79 ± 0.03	190.3 ± 26.3	10.54 ± 0.27^	10
NQ596	*nlp-22*(*gk509904*)X	-	55.3 ± 5.4**	0.67 ± 0.04*	139.5 ± 29.6**	10.74 ± 0.72^	10
NQ596	*nlp-22*(*gk509904*)X	-	49.3 ± 5.5	0.57 ± 0.04	141.9 ± 21.7	-	11
NQ603	*nlp-22*(*gk509904*)X	***qnEx311*[*nlp-22*(+);*myo:Cherry*;*unc-119*(+)]**	81.3 ± 9.0**	0.68 ± 0.05	246.1 ± 16.1**	-	11
NQ305	*sid-1*(*pk3321*)V	***qnIs137[dpy-7:nlp-22(RNAi);myo-2>mCherry;unc-119(+)]***	100.3 ± 9.2	0.82 ± 0.03	205.1 ± 37.6	-	11
NQ376	*sid-1*(*pk3321*)V	***qnIs157[glr-3:nlp-22(RNAi);myo-2:mCherry;unc-119(+)]***	61.5 ± 5.4**	0.67 ± 0.15*	163.6 ± 34.9*	-	11
NQ156	*lin-15*(*n765ts*)X	***qnEx48*[P*ins-4:gfp;lin-15*(+)]**	101.2 ± 9.9	0.78 ± 0.06	220.9 ± 16.4	-	9
VM1345	*lin-15*(*n765ts*)X	**(2 RIAs DEAD) *akEx211*[P*glr-3:gfp;*P*glr-3:ICE;lin-15*(+)]**	62.4 ± 8.9**	0.66 ± 0.06*	192.2 ± 17.2*	-	9
NQ156	*lin-15*(*n765ts*)X	***qnEx48*[P*ins-4:gfp;lin-15*(+)]**	114.4 ± 14.7	0.86 ± 0.03	229.2 ± 11.7	-	6
VM1345	*lin-15*(*n765ts*)X	**(1 RIA DEAD) *akEx211*[P*glr-3:gfp;*P*glr-3:ICE;lin-15*(+)]**	96.7 ± 9.7*	0.83 ± 0.05	198.5 ± 26.2	-	6

Supplementary Table S2: Quiescence measurements. (Student's two-tailed *t*-Test. **p<0.005;*p<0.05) Data is from 8 worms only since 2 of the 10 worms were monitored starting only in L4 larval stage. Total quiescence and peak fraction quiescence measurements shown are the average ± standard error of the mean. Lethargus duration and duration between L3 and L4 lethargus measurements are the average ± standard deviation. Measurements were made in a paired fashion. Therefore, there are two rows describing *nlp-22(gk509904)* data, one paired with simultaneously recorded wild-type data and one paired with simultaneously recorded data from *nlp-22(gk509904)*; qnEx311. Data from paired experiments is listed in consecutive rows shaded in the same color (gray or white). The strain NQ156, which was used as a *lin-15* transgenic control for VM1345, carries a transgene array with a GFP reporter expressed in a small set of neurons.

Oligo Name	Description	Sequence
	P*hsp-16.2*:*nlp-22*	
oNQ366	For- *nlp-22* - Adds Heat Shock Promoter tail	CTTCGAAAATCCTCATCGGATCCATGCGTTCCATAATCGTC
oNQ367	Rev - Past 3'UTR of *nlp-22*	GTGAAGTAGCGCCAGTG
oNQ368	Nested to oNQ367	AAGACATGGTTATGGCAC
oNQ372	For - HSPr from Fire Vector pPD49.83	GCCAAGCTTGCATGCCTG
oNQ373	Nested to oNQ372	CAGGTCGACTCTAGAGG
oNQ374	Rev- HSPr from Fire Vector pPD49.83	GGATCCGATGAGGATTTTC
	P*nlp-22*:*nlp-22*::*gfp*	
oNQ416	For - *nlp-22* promoter	TATCAGTCGTCAAGGATTCCG
oNQ417	Nested to oNQ416	TCAATGCCATTTGCAGAGAG
oNQ470	Rev - Before stop codon - Adds GFP tail	AAAAGTTCTTCTCCTTTACTCATTACTCCGATTGGGAATCCAGTT
oNQ471	For - GFP in pPD95.75 - Adds *nlp-22* tail	AACTGGATTCCCAATCGGAGTAATGAGTAAAGGAGAAGAACTTTT
oNQ472	Rev - In *unc-54* 3'UTR in pPD95.75	AAAAGAAGCTAAAAAACAAAGAAATTA
oNQ473	Nested to oNQ472	GAGAAGTTTTTTGATAATAACAAAAATAGG
	Mutated versions of P*hsp-16.2*:*nlp-22* (Each pair (646-720) was used with oNQ366 and oNQ367, respectively)	
oNQ541	For- Used with oNQ367	AAATCTTCAAACTATAATCATGCAGACCTCAGCTCTTGGGCTTCAG
oNQ646	Rev - Mutates KR to AA	CGTTGTTGCTGCCCCTGGACGGAATCCGGCTCG
oNQ647	For - Mutates KR to AA	CAGGGGCAGCAACAACGGACGAACTAACTGGATT
oNQ711	For - FRPG to MRPG	ATGCGTCCAGGGAAACGAACAACG
oNQ712	Rev - FRPG to MRPG	TTGTTCGTTTCCCTGGACGCATTCCGGCTCGCCCAATCGCAATC
oNQ713	For - FRPG to FEPG	TCGAACCAGGGAAACGAACAACGGAC
oNQ714	Rev - FRPG to FEPG	GTTTCCCTGGTTCGAATCCGGCTCGCCCAATCGCA
oNQ715	For - FRPG to FREG	CGTGAAGGGAAACGAACAACGGACGAA
oNQ716	Rev - FRPG to FREG	GTTGTTCGTTTCCCTTCACGGAATCCGGCTCGCCCAAT
oNQ717	For - FRPG to FRPE	TCCAGAAAAACGAACAACGGACGAACTA
oNQ718	Rev - FRPG to FRPE	CGTTGTTCGTTTTTCTGGACGGAATCCGGCTCGCCC
	P*nlp-22*:*gfp*::*nlp-22*	
0NQ556	For - GFP in pPD95.75 - Used with oNQ559	TTTCCCAACTCGGAAATGAGTAAAGGAGAAGAACTT
oNQ557	Rev - *nlp-22* promoter - Used with oNQ416	AAAAGTTCTTCTCCTTTACTCATTTCCGAGTTGGGAAAGTTCGAG
oNQ558	For - *nlp-22* - Used with oNQ367	ATGGCATGGATGAACTATACAAAATGCGTTCCATAATCGTCTTC
oNQ559	Rev - GFP (before stop)	ATGAAGACGATTATGGAACGCATTTTGTATAGTTCATCCATGCC
	P*glr-3*:*nlp-22*(RNAi)	
oNQ533	For - *nlp-22* coding sequence for RNAi	TTAGCTTTACACAATGTTAAAGGAAAA
oNQ534	Rev - *nlp-22* coding sequence for RNAi	AACAATTAACATCAGAAAATTCATACT
oNQ535	Rev - Nested to oNQ534 for sense - with 616	ATTAACATCAGAAAATTCATACTCCG
oNQ536	Rev - Nested to oNQ534 for anti - with 616	GCTTTACACAATGTTAAAGGAAAAG
oNQ615	For - *glr-3* promoter	CTTCAATCTTCAAAAAAGGGCATT
oNQ616	Nested to 615	CTTCAAAAAAGGGCATTAAAAACAGT
oNQ641	Rev - *glr-3* promoter - Adds sense tail	TTTTCCTTTAACATTGTGTAAAGCTAAAATCCAGAACATATGTTAATAGCAAA
oNQ642	Rev - *glr-3* promoter - Adds antisense tail	AGTATGAATTTTCTGATGTTAATTGTTAATCCAGAACATATGTTAATAGCAAA
	P*glr-3*:*mCherry*	

oNQ856	Rev - *glr-3* promoter - used with 615	GAAAAGTTCTTCTCCTTTACTCATAATCGCAATCGACTTTTTCATGAT
oNQ857	For - mCherry from pCFJ90 - used with 472	CTTTTTTGTACAAACTTGTCATGAACATATGTTAATAGCAAATATT
		P*dpy-7*:*nlp-22*(RNAi)
oNQ567	For - *dpy-7* promoter	CAGCAGCGGTAACGGAGACAT
oNQ568	Nested to 567	GGTAACGGAGACATCAGTGACCT
oNQ569	Rev - *dpy-7* promoter - Adds sense tail	TTTTCCTTTAACATTGTGTAAAGCTAATTATCTGGAACAAAATGTAAGAATA
oNQ570	Rev - *dpy-7* promoter - Adds antisense tail	AGTATGAATTTTCTGATGTTAATTGTTTTATCTGGAACAAAATGTAAGAATA
		P*nlp-22*(w/Intron):*gfp*
oNQ648	Rev - GFP - Adds *nlp-22* intron tail - with 557	TTGTGTAAAGCTAACGTGTCTTGTAGTTCCCGTCAT
oNQ649	For - Intron *nlp-22* -Adds gfp tail - with 650	GGGAACTACAAGACACGTTAGCTTTACACAATGTTA
oNQ650	Rev - intron *nlp-22* -Adds gfp tail	ACCTGAAATTACGGTGCTTGTTG
oNQ651	For - GFP - Adds *nlp-22* intron tail - with 472	ACCGTAATTTCAGGTGCTGAAGTCAAGTTTGAAG
		P*glr-3*:ChannelRhodopsin-2
oNQ617	Rev - *glr-3* promoter ChR2 tail - with 615	CAGGGCGCCTCCATAATCCATAATCCAGAACATATGTTAATAGCAAA
oNQ618	For - ChR2 *glr-3* tail - with 472	AATATTTGCTATTAACATATGTTCTGGATTATGGATTATGGAGGCGCCCTG
		Sequencing *gk509904*
oNQ552	Forward	GGATTGACGATCTTCGCGTTG
oNQ534	Reverse	AACAATTAACATCAGAAAATTCATACT
		P*hsp-16.2*:Human NMS(17-33)
oNQ1167	Rev - engineers NMS(17-33) in nlp-22 - with 366	AAGGAAGAATGGGCGTCCCCAGGTGGCGGTGTGGTCCTTTTTCATGATTGGAAGGGTTCG
oNQ1168	For - engineers NMS(17-33) in nlp22 - with 367	ACCTGGGGACGCCCATTCTTCCTTTTCCGCCCACGTAACGGGAAACGAACAACGGACGAA
		***nlp-22* qPCR**
	Probe	/56-FAM/AAGCGCCCC/ZEN/TCACGAGTGT/3IABkFQ/
	Primer 1	ATCCTTCACCGAGCAAACTAC
	Primer 2	ATGATTGGAAGGGTTCGGAG

Supplementary Table S3: Oligonucleotides used in this study. DNA constructs were made using overlap-extension PCR[48]. Mutated versions of *nlp-22* were made by PCR and then TOPO© cloned into a pCR™2.1-TOPO® TA Vector (Invitrogen™). They were sequenced to verify that the intended mutation was successfully introduced and that no additional mutations were introduced.