A	С			
WT egl-3 WT egl-21 bp				
-500 -500 -500	Genes	Target Sites	PAM	
	<i>ins-17</i>	TGTCCCGAGTGATTGGAGC	CGG	
	INS-34	TTGTAGTCGGGGGCTGGAGT	TGG	
	flp-2	CTGTCAACGACAACACTCT	TGG	
	flp-15	TAAAGAAAGGCGGACCCCA	GGG	
	nlp-10	TGGTACATCGCTCTCTTGT	TGG	
	nlp-28	CTACCAGTGCTCAGTGGGGA	TA TGG	
В				
genes	over 1/2 UPR mt	genes ov	er ½ UPR mt	
daf-28, ins -24, ins -25	69%	flp-10, flp -23, nlp -5	55%	
ins - 1, ins -22, ins -26	55%	flp-12, flp-13, flp-14	78%	
ins -2, nlp -41, nlp -42	43%	flp-16, flp-17, flp-18	75%	
ins -3, ins -5, ins -9	58%	flp-20, flp-21, flp-22	74%	
ins -4, ins -23, nlp -18	65%	flp-26, flp-27, flp-28	69%	
ins -7, ins -10, ins -12	50%	flp-32, flp-33,flp-34	77%	
ins - 11, ins - 15, ins - 16	88%	nlp-1, nlp-2, nlp-6	26%	
ins - 13, ins - 14, ins - 21	33%	nlp-7, nlp-8, nlp-15	58%	
ins - 17, ins - 18, ins - 19	37%	nlp-9, nlp-10, nlp-11	40%	
ins -27, ins -28, ins -32	55%	nlp-13, nlp -20, nlp -35	45%	
ins -29, ins -36, ins -37	38%	nlp-19, nlp -29, nlp -30	34%	
ins - 30, ins - 31, ins - 33	72%	nlp-24, nlp -25, nlp -26	55%	
ins -34, ins -35, ins - 20	37%	nlp-27, nlp -31, nlp -32	46%	
ins -38, flp -4, flp -6	58%	nlp-33, nlp -34, nlp -37	52%	
flp-1, flp-3, nlp-14	69%	nlp-38, nlp -39, nlp -40	29%	
flp-2, flp -5, flp -19	38%	ins -6, ins -8	93%	
flp-2, flp-15, nlp-28	34%	flp-24, flp -25	67%	
flp-7, flp-8, flp-9	47%			
D	E			
control flp-2-sg		N2 control RNAi N2 spg-7 RNAi		
bp 4 *** atfs-1 control F			ontrol RNAi	
-600	£2 -		**	
-400	. <u></u> 2		1	
-300	ange		. i i i	
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	높이 [flp-2 flp-15 nlp-	-10 nlp-28	
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Supplementary Figure 5 Cell non-autonomous UPR^{mt} signaling requires
neuropeptides. (A) Representative DNA gel shows PCR products of wild-type, *egl-3* or *egl-21* mutant. (B) Quantification of *hsp-6p::*GFP reporter induction in animals
expressing *rab-3p*::Cas9+*u6p*::*spg-7*-sg with the deletion of random three
neuropeptide genes in the nervous system. (C) Targeting sequences for CRISPR-Cas9 knockout of each indicated neuropeptide gene, together with their PAM
sequences. (D) *flp-2* deletion produced by CRISPR/Cas9 is detected by T7E1
assay. Representative DNA gel of T7E1 assay shows the PCR products amplified
from genomic DNA of control worms, or worms with *flp-2* knockout in the nervous

system. (**E**) Fold changes of neuropeptide gene transcripts fed with control RNAi or *spg-7* RNAi in *N2* vs. *atfs-1(tm4525)* strain. Error bars indicate mean ±SE. A Student's t-test is used to assess significance. *p < 0.05,**p < 0.01,***p < 0.001.