



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 \pm SE. A Student's t-test is used to assess significance. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.