

**Supplemental Information**

**Differential neuropeptidomes of dense core secretory vesicles (DCSV) produced at intravesicular and extracellular pH conditions by proteolytic processing**

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## Supplemental Information List

### PDF File:

**Figure S1.** Proteomics data assessed by GO (gene ontology) function (A) and relative abundance (calculated by normalized spectral abundance factor (NSAF)) of identified proteins as protease and proneuropeptide components (B).

**Figure S2.** CHGA-derived neuropeptidomes at pH 5.5 and pH 7.2, in the presence of pepstatin, E64c, AEBSF, and EDTA protease inhibitors.

**Figure S3.** CHGB-derived neuropeptidomes at pH 5.5 and pH 7.2, in the presence of pepstatin, E64c, AEBSF, and EDTA protease inhibitors.

**Figure S4.** PENK-derived neuropeptidomes at pH 5.5 and pH 7.2, in the presence of pepstatin, E64c, AEBSF, and EDTA protease inhibitors.

**Figure S5.** SCG3-derived neuropeptidomes at pH 5.5 and pH 7.2, in the presence of pepstatin, E64c, AEBSF, and EDTA protease inhibitors.

**Figure S6.** SCG2-derived neuropeptidomes at pH 5.5 and pH 7.2, in the presence of pepstatin, E64c, AEBSF, and EDTA protease inhibitors.

**Figure S7.** ADM-derived neuropeptidomes at pH 5.5 and pH 7.2, in the presence of pepstatin, E64c, AEBSF, and EDTA protease inhibitors.

**Figure S8.** PCSK1N-derived neuropeptidomes at pH 5.5 and pH 7.2, in the presence of pepstatin, E64c, AEBSF, and EDTA protease inhibitors.

**Figure S9.** VGF-derived neuropeptidomes at pH 5.5 and pH 7.2, in the presence of pepstatin, E64c, AEBSF, and EDTA protease inhibitors.

**Figure S10.** SCG5-derived neuropeptidomes at pH 5.5 and pH 7.2, in the presence of pepstatin, E64c, AEBSF, and EDTA protease inhibitors.

**Figure S11.** NPY-derived neuropeptidomes at pH 5.5 and pH 7.2, in the presence of pepstatin, E64c, AEBSF, and EDTA protease inhibitors.

**Figure S12.** GAL-derived neuropeptidomes at pH 5.5 and pH 7.2, in the presence of pepstatin, E64c, AEBSF, and EDTA protease inhibitors.

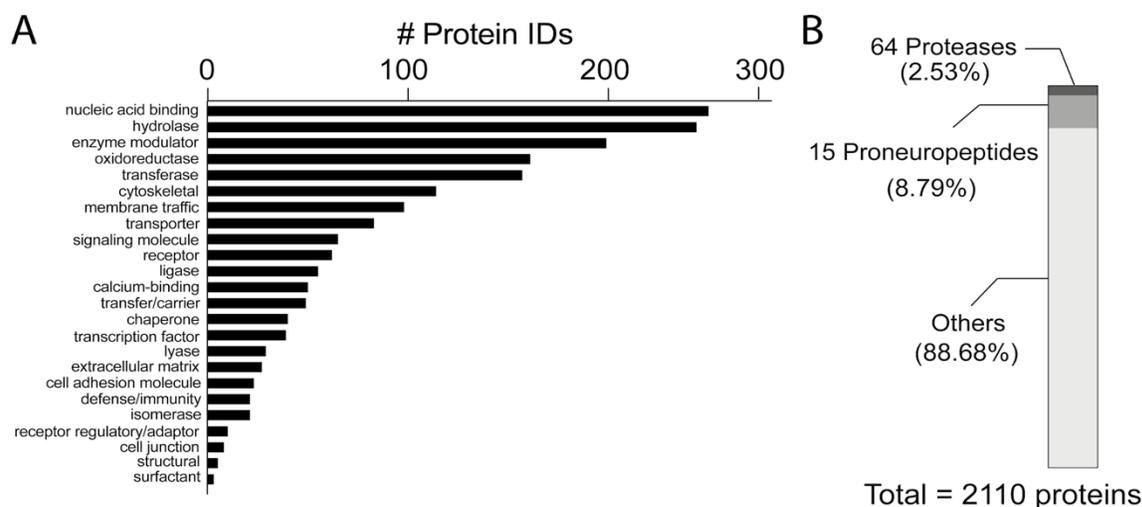
**Figure S13.** NPPA-derived neuropeptidomes at pH 5.5 and pH 7.2, in the presence of pepstatin, E64c, AEBSF, and EDTA protease inhibitors.

**Figure S14.** Volcano plots of peptidomics analysis of CG neuropeptidomes generated at pH 5.5 and pH 7.2 in the presence of DMSO (control), pepstatin, E64c, AEBSF, or EDTA.

### Excel Files:

Supplementary data 1. CG raw data

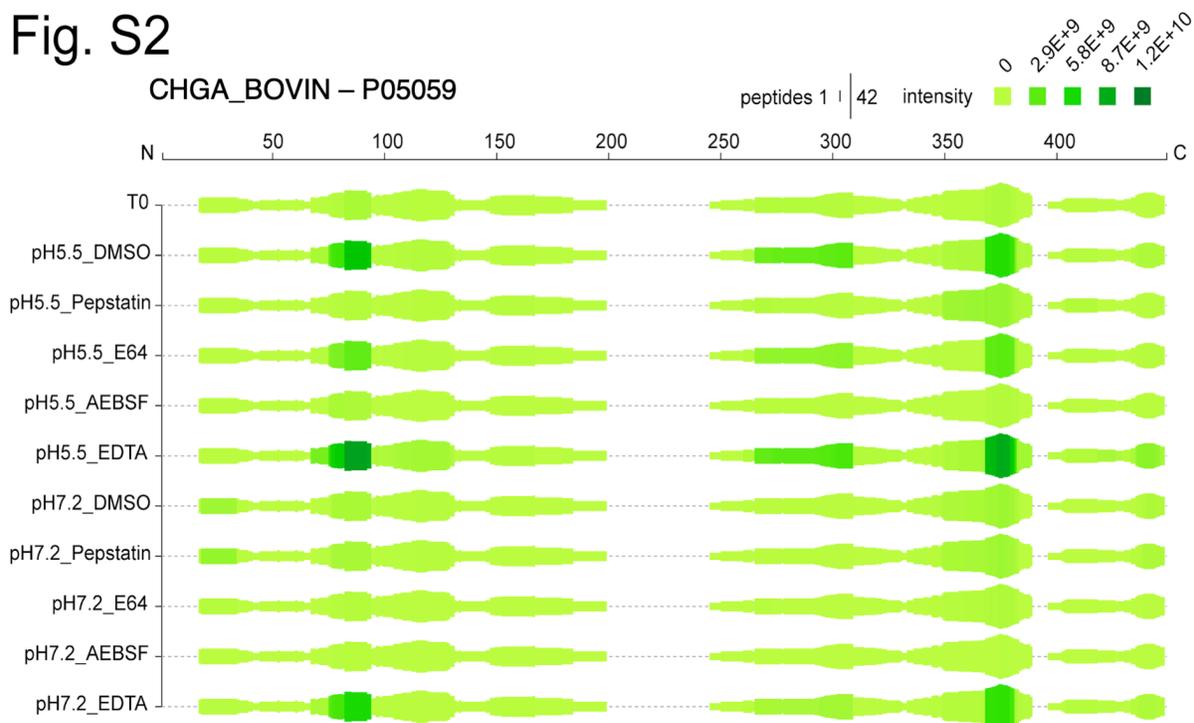
Supplementary data 2. CG Figures



**Figure S1.** Proteomics data assessed by GO (gene ontology) function (A) and relative abundance (calculated by normalized spectral abundance factor (NSAF)) of identified proteins as protease and proneuropeptide components (B).

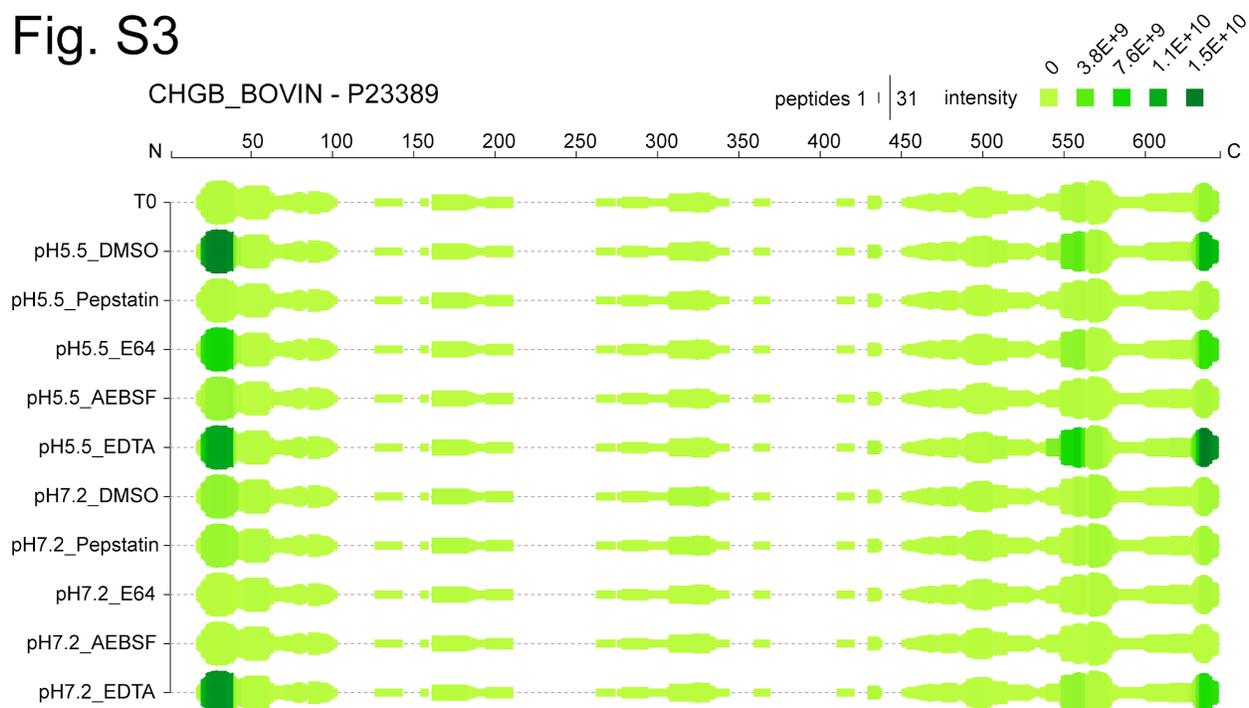
**Figures S2-S13.** Heatmaps of 12 proneuropeptide peptidome profiles, compiled from peptidomics data after 90 min incubation with addition of different inhibitors. For each amino acid of proneuropeptides, the height of the green bars is proportional to the number of amino acids overlapping this region. The darkness of the color is proportional to the sum of the peptide intensities.

**Fig. S2**



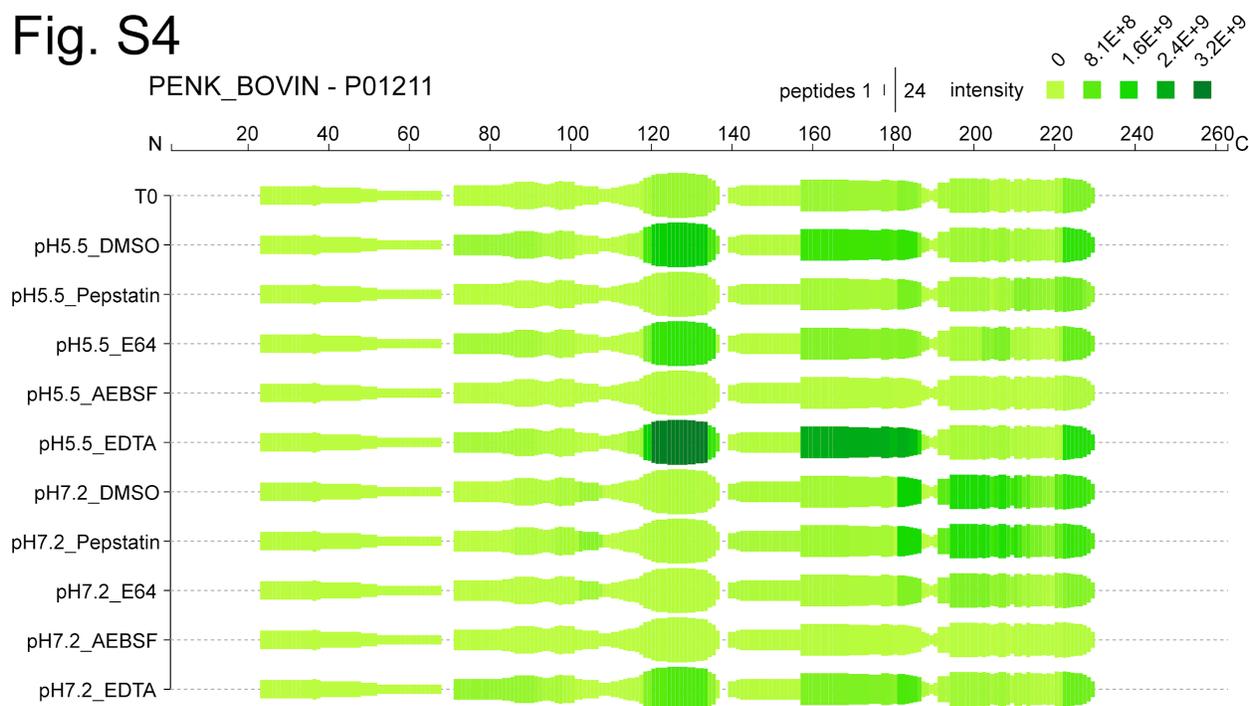
**Figure S2.** CHGA-derived neuropeptidomes at pH 5.5 and pH 7.2, in the presence of pepstatin, E64c, AEBSF, and EDTA protease inhibitor.

Fig. S3



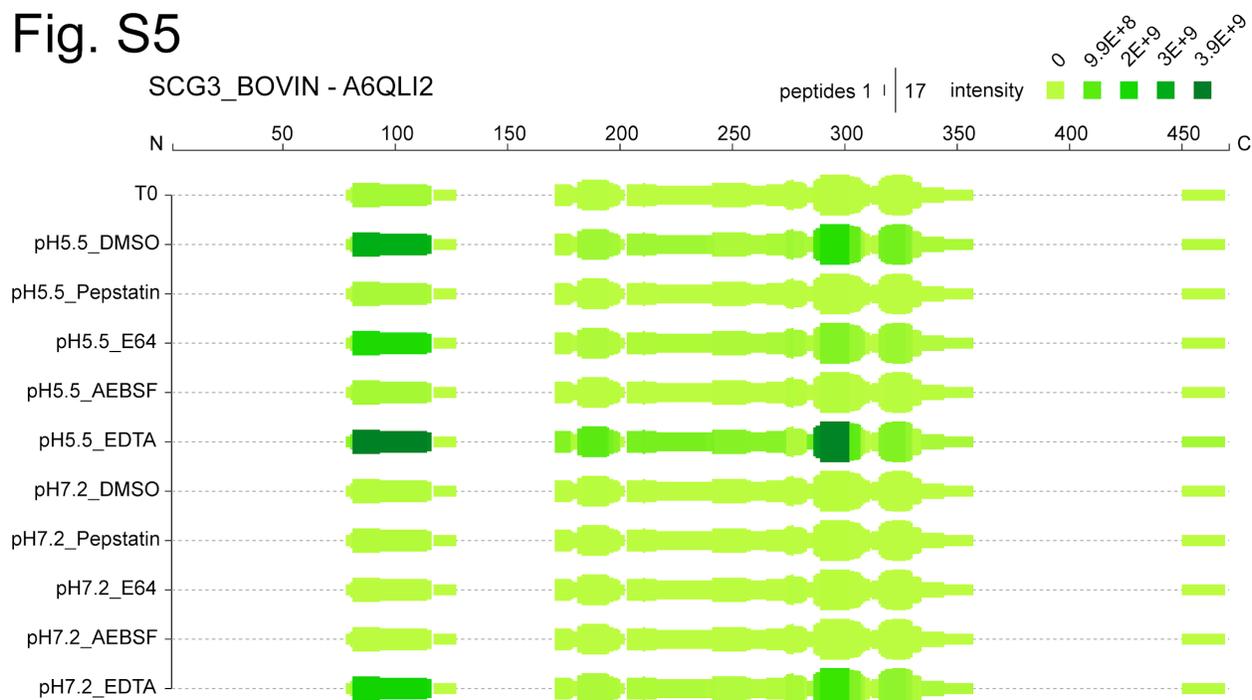
**Figure S3.** CHGB-derived neuropeptidomes at pH 5.5 and pH 7.2, in the presence of pepstatin, E64c, AEBSF, and EDTA protease inhibitors.

Fig. S4



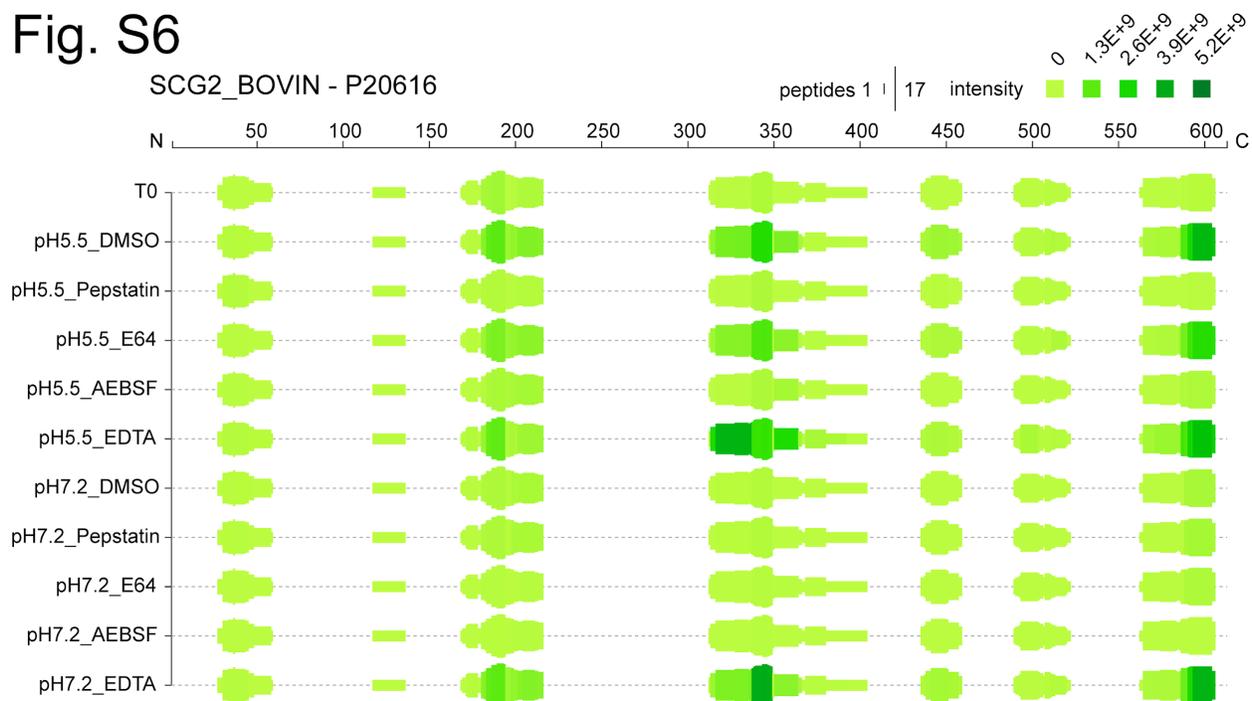
**Figure S4.** PENK-derived neuropeptidomes at pH 5.5 and pH 7.2, in the presence of pepstatin, E64c, AEBSF, and EDTA protease inhibitors.

Fig. S5



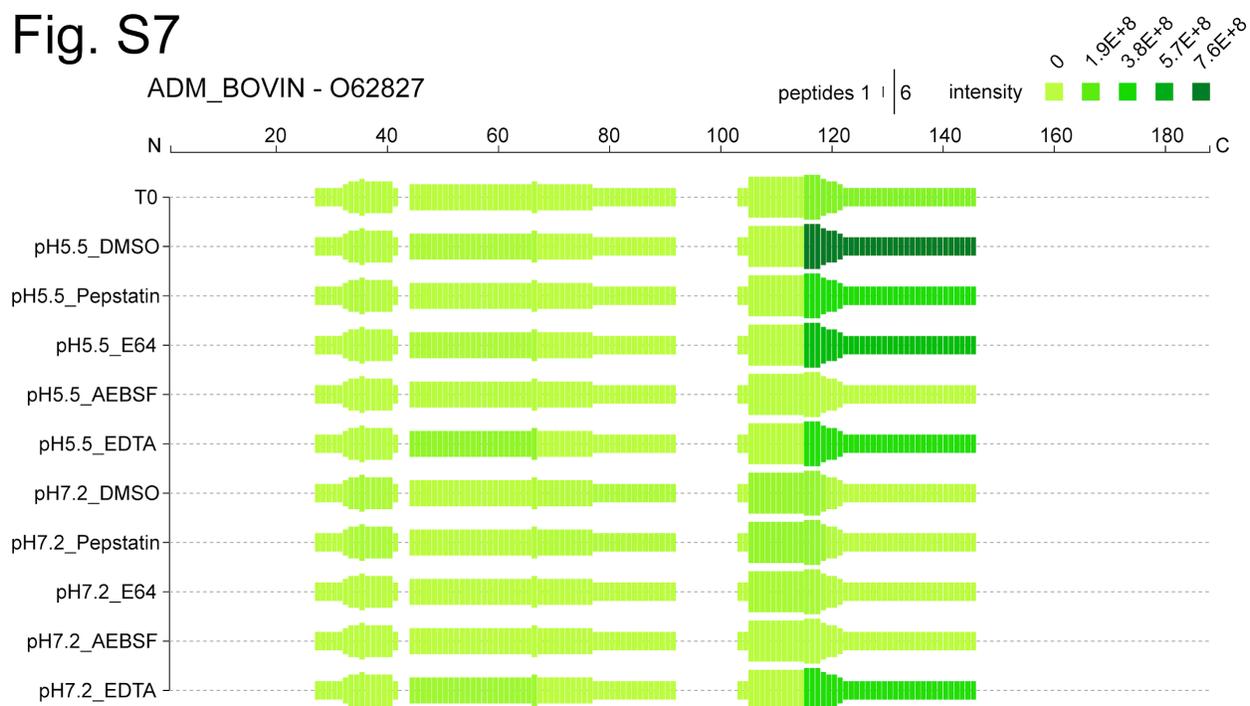
**Figure S5.** SCG3-derived neuropeptidomes at pH 5.5 and pH 7.2, in the presence of pepstatin, E64c, AEBSF, and EDTA protease inhibitors.

Fig. S6



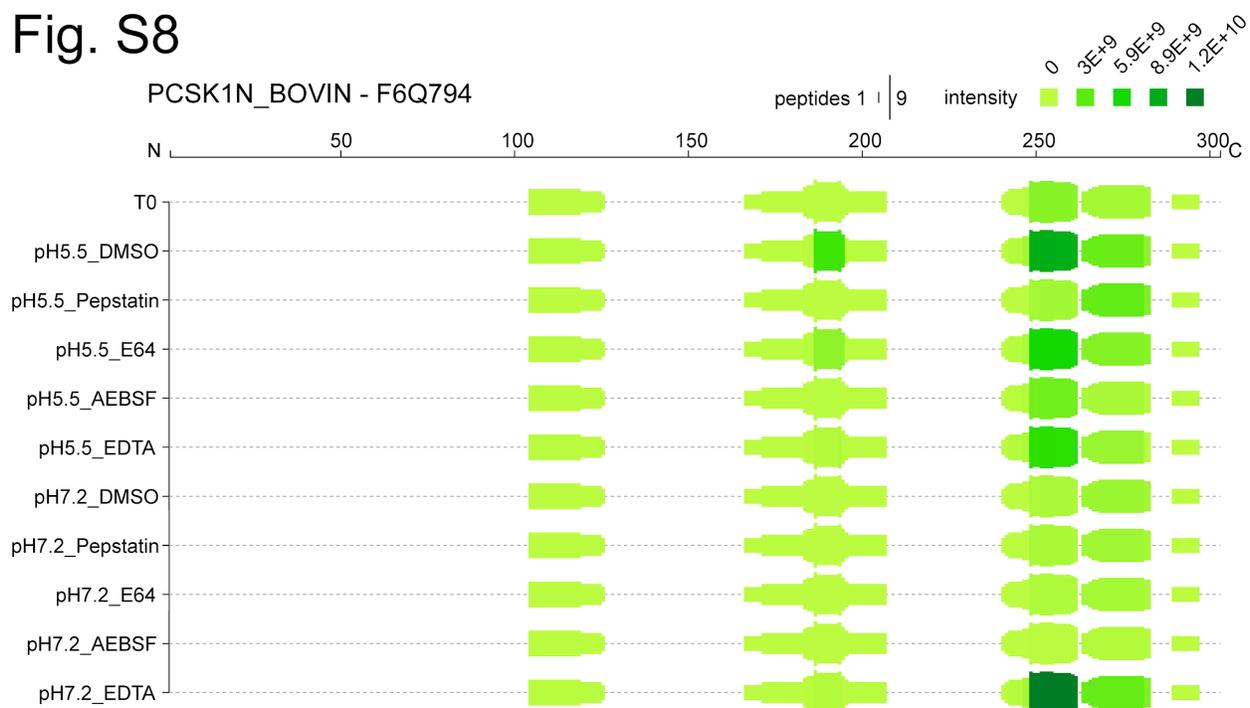
**Figure S6.** SCG2-derived neuropeptidomes at pH 5.5 and pH 7.2, in the presence of pepstatin, E64c, AEBSF, and EDTA protease inhibitors.

Fig. S7



**Figure S7.** ADM-derived neuropeptidomes at pH 5.5 and pH 7.2, in the presence of pepstatin, E64c, AEBSF, and EDTA protease inhibitors.

Fig. S8



**Figure S8.** PCSK1N-derived neuropeptidomes at pH 5.5 and pH 7.2, in the presence of pepstatin, E64c, AEBSF, and EDTA protease inhibitors.

Fig. S9



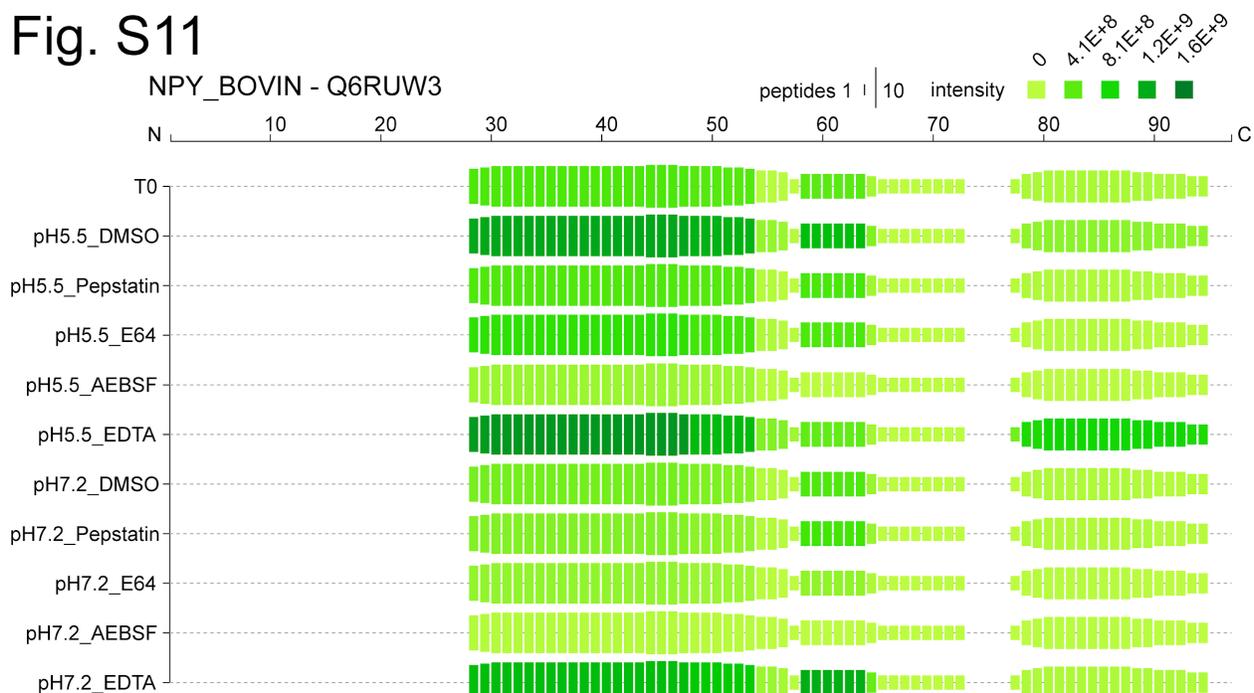
**Figure S9.** VGF-derived neuropeptidomes at pH 5.5 and pH 7.2, in the presence of pepstatin, E64c, AEBSF, and EDTA protease inhibitors.

Fig. S10



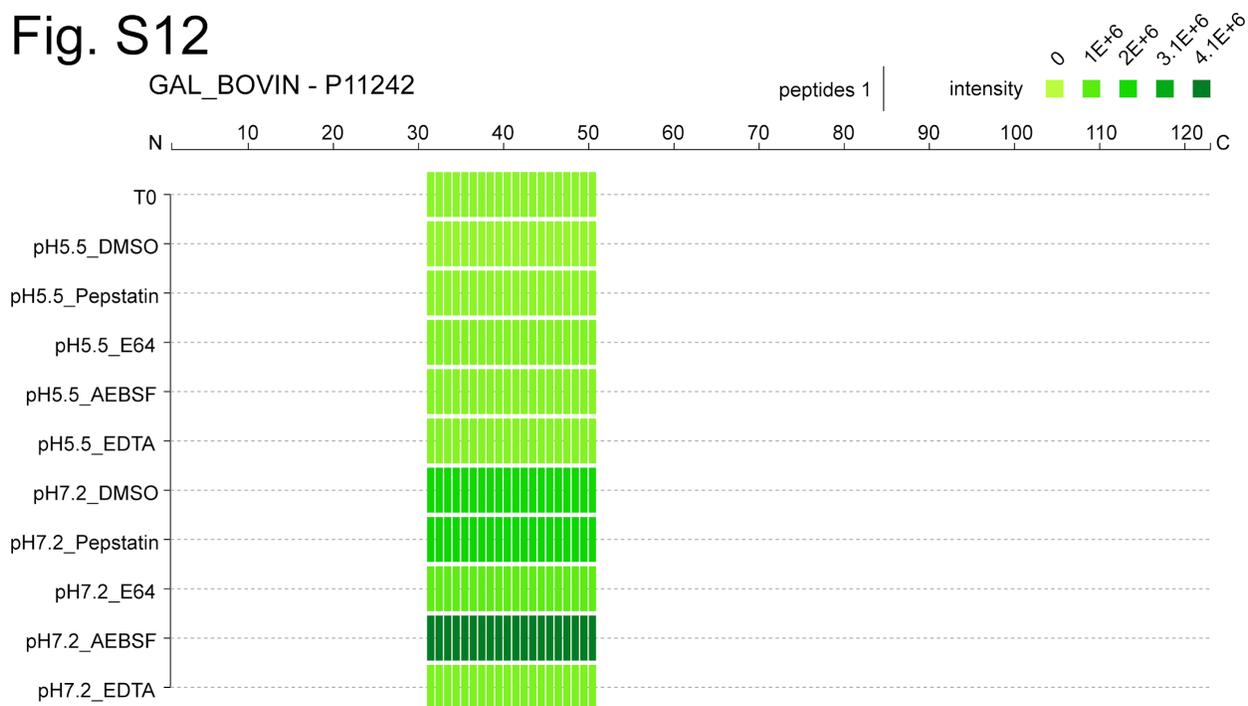
**Figure S10.** SCG5-derived neuropeptidomes at pH 5.5 and pH 7.2, in the presence of pepstatin, E64c, AEBSF, and EDTA protease inhibitors.

Fig. S11



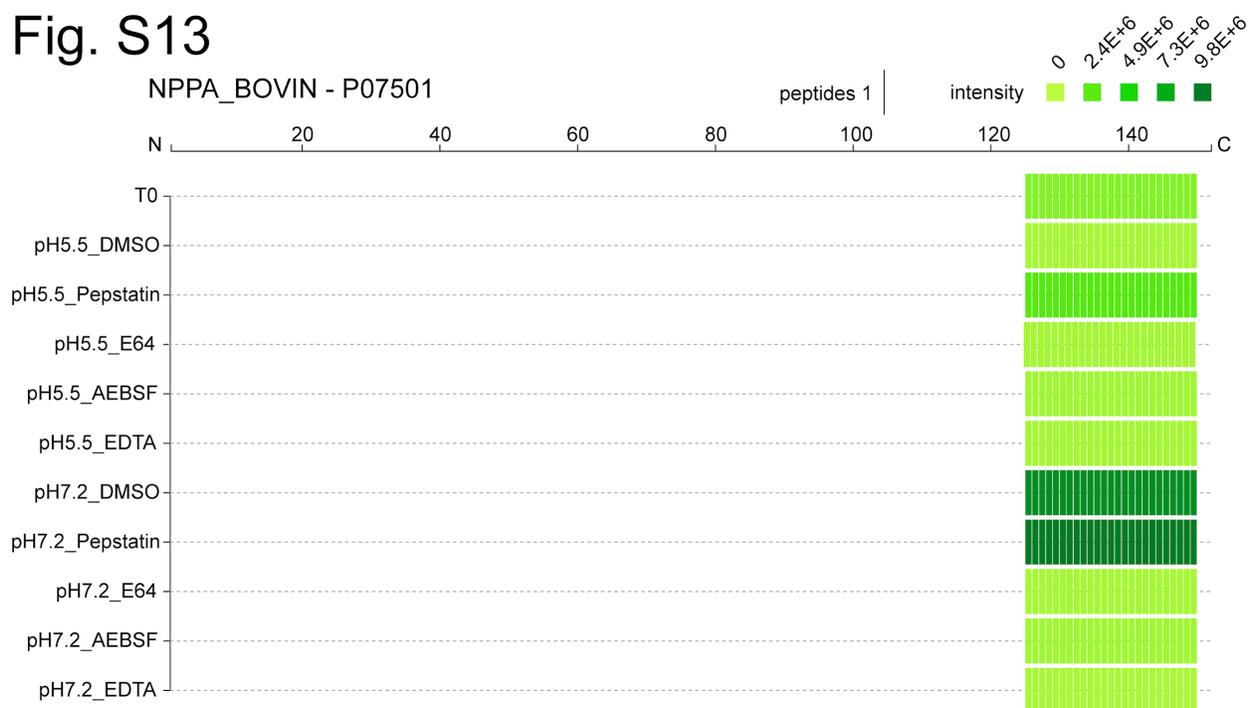
**Figure S11.** NPY-derived neuropeptidomes at pH 5.5 and pH 7.2, in the presence of pepstatin, E64c, AEBSF, and EDTA protease inhibitors.

Fig. S12

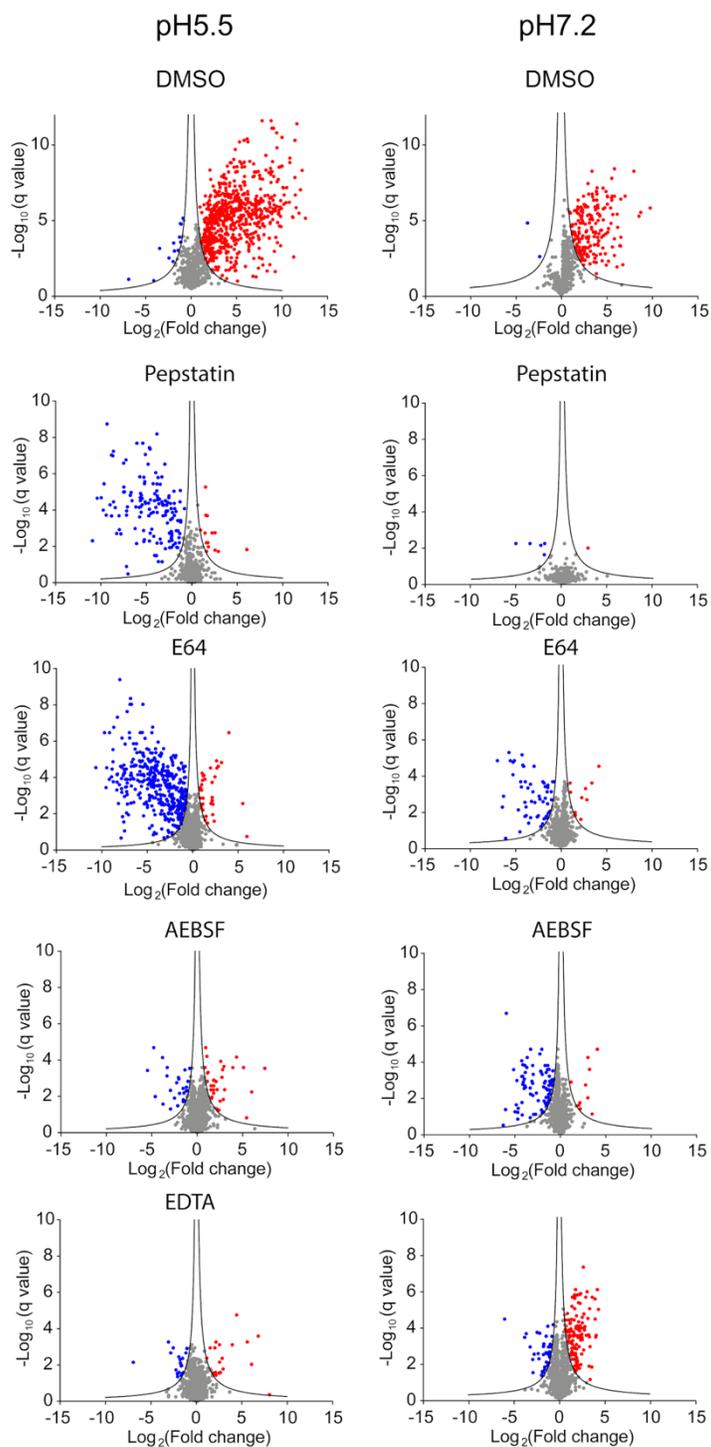


**Figure S12.** GAL-derived neuropeptidomes at pH 5.5 and pH 7.2, in the presence of pepstatin, E64c, AEBSF, and EDTA protease inhibitors.

Fig. S13



**Figure S13.** NPPA-derived neuropeptidomes at pH 5.5 and pH 7.2, in the presence of pepstatin, E64c, AEBSF, and EDTA protease inhibitors.



**Figure S14.** Volcano plots of peptidomics analysis of CG neuropeptidomes generated at pH 5.5 and pH 7.2 in the presence of DMSO (control), pepstatin, E64c, AEBSF, or EDTA.