







### Supplemental Table 1

## Supplemental Table 1. Pancreatic tissue parameters in supramaximal cerulein-induced pancreatitis

	Group	MPO UMPO/mg DNA	Active Trypsin nmoles/mg DNA	NF-kB (p65) ug/mg DNA	NF-kB (p50) ug/mg DNA	LPO nmol/mg DNA	MDA umol/mg DNA
VAMP-8 <sup>+/+</sup>	Control	0±0	0.16±0.07	below detection limit	below detection limit	below detection limit	0.79±0.10
	Cerulein	21.05±0.84	5.48±0.29	439±25	6.13±0.10	357±33	25.21±0.23
VAMP-8 <sup>-/-</sup>	Control	0±0	0.11±0.04	below detection limit	below detection limit	below detection limit	0.75±0.08
	Cerulein	7.32±0.94 *	4.17±0.16	176±18 *	2.85±0.14 *	130±16 *	16.03±0.15 *

### Supplemental Table 2

## Supplemental Table 2. Serum parameters in supramaximal cerulein-induced pancreatitis

	Group	Amylase (IU/L)	Lipase (IU/L)	IL-6 (pg/mL)	TNFα (pg/mL)	MIP-1 α (pg/mL)
VAMP-8 <sup>+/+</sup>	Control	Control 583±11		below detection limit	below detection limit	7±2
	Cerulein	5689±48	4115±29	1144±39	523±32	991±42
VAMP-8 <sup>-/-</sup>	Control	525±19	16±2	below detection limit	below detection limit	5±0.7
	Cerulein	2864±33 *	1806±28 *	699±12 *	273±39 *	611±21 *

## Supplemental Table 3. Histopathological score in supramaximal cerulein-induced pancreatitis

	Group	Edema	Hemorrhage	Infiltrate	Necrosis
	Control 0±0		0±0	0±0	0±0
	Cerulein	1.17±0.09	3.11±0.15	2.51±0.12	3.31±0.2
VAMP-8 <sup>-/-</sup>	Control	0±0	0±0	0±0	0±0
	Cerulein	0.97±0.05 *	1.54±0.16 *	1.17±0.09 *	1.32±0.14 *

## Supplemental Table 4. Lung tissue parameters and histopathological score in supramaximal cerulein-induced pancreatitis

	Group	Edema	Hemorrhage	Leukocyte Infiltrate	MPO UMPO/mg DNA	NF-kB (p65) ug/mg DNA	NF-kB (p55) ug/mg DNA
VAMP-8 <sup>+/+</sup>	Control	0±0	0±0	0±0	0±0	below detection limit	below detection limit
	Cerulein	2.2±0.3	3.7±0.6	2.1±0.8	13.0±0.4	315±46	3.3±0.50
VAMP-8 <sup>-/-</sup>	Control	0±0	0±0	0±0	0±0	below detection limit	below detection limit
	Cerulein	0.8±0.1 *	1.6±0.5 *	1.1±0.3 *	5.6±1.0 *	108±12 *	1.5±0.14 *

#### **Supplementary Data**

**Supplemental Figure 1:** Summary of the NIH-Image densitometry analysis of the data from **Figure 3A** showing VAMP-8, VAMP-2 and actin levels in pancreatic acini of VAMP-8<sup>+/+</sup> and VAMP-8<sup>-/-</sup> mice. The data was from three independent experiments, with samples performed in duplicates. \*: p < 0.05.

Supplemental Figure 2: Morphometric analysis of EM of pancreatic tissues of CD- and EDfed VAMP-8<sup>+/+</sup> and VAMP-8<sup>-/-</sup> mice: ZG abundance, distribution, fusion events, and apical lumen area. The data shown is the analysis of the EM images shown in Figs. 6 and 7. A) Number of ZGs per EM cell section. B) Distribution of ZGs within the acinar cell section. X axis indicates the distance from the apical lumen. C) Number of ZGs per cell section docked on the lateral PM (LPM). D) Distribution of ZGs per cell section docked on the LPM. X axis indicates the distance from the junctional complex. E) Number of ZG-ZG fusions per EM cell section. F) Apical lumen areas. For each strain and treatment, 300 cells from 3 independent experiments were quantified. Data are expressed as means  $\pm$  SD; statistical significance was examined by Mann-Whitney U-test (non-parametric) for ZGs analysis and Student *t* test for apical lumen areas. \*: p<0.05 and \*\*: p<0.01 compared to CD/Saline.

**Supplemental Figure 3:** Summary of the NIH-Image densitometry analysis of the data from **Figure 9**, which are immunoprecipitated Syntaxin-4 (in **A**) and Syntaxin-2 (in **B**) from PM fractions, and immunoprecipitated Syntaxin-3 from ZG membrane fractions (in **C**) prepared from pancreatic acini stimulated by the indicated treatment conditions. VAMP-8<sup>+/+</sup> and VAMP-8<sup>-/-</sup>

mice acini were used in **A**, whereas only VAMP-8<sup>+/+</sup> mice acini were used in **B** and **C**. The data came from blots of three independent experiments, with samples performed in duplicates. Data is expressed as means  $\pm$  SD; \*: p <0.05 compared to KRH.

# Supplemental Table 1: Pancreatic tissue parameters in supramaximal cerulein-induced pancreatitis.

\*: p < 0.05 compared to VAMP-8<sup>+/+</sup> mice.

Supplemental Table 2: Serum parameters in supramaximal cerulein-induced pancreatitis. \*: p<0.05 compared to VAMP-8<sup>+/+</sup> mice.

# Supplemental Table 3: Histopathological score in supramaximal cerulein-induced pancreatitis.

\*: p<0.05 compared to VAMP- $8^{+/+}$  mice.

Supplemental Table 4: Lung tissue parameters and histopathological score in supramaximal cerulein-induced pancreatitis.

\*: p<0.05 compared to VAMP- $8^{+/+}$  mice.