**SUPPLEMENTAL FIGURE 1. PAR2 deletion does not alter the outcome of diet-induced pancreatitis.** Nineteen female wild type (wt) and 11 female  $PAR2^{-/-}$  mice weighing 13-15g were fasted for 24 hrs and then fed the choline-deficient, ethionine-supplemented diet for 3 days to induce pancreatitis. The animals were then observed for an additional 3 days during which time animal mortality rate was monitored. The 2- and 3-day cumulative animal mortality rates in each group, expressed as a percent of total animals in that group, are shown..

#### SUPPLEMENTAL FIGURE 2. PAR2 deletion does not alter in-vitro trypsinogen

activation induced by either Na-taurocholate or caerulein. Acini (5-100 cells per cluster) from wild type and  $PAR2^{-/-}$  mice were incubated with 0.3% Na-taurocholate (NaT) for 5 min or 10 nM caerulein (caer) for 30 minutes. Trypsinogen activation was quantitated by measuring trypsin activity using the fluorogenic substrate Boc-gln-ala-arg-MCA. No significant difference between the wild type and  $PAR2^{-/-}$  acini was noted.

**SUPPLEMENTAL FIGURE 3. PAR2 deletion does not alter the frequency with which the calcium transient patterns are observed in wild type acini exposed to caerulein.** Small pancreatic acini (1-10 cells per cluster) were freshly prepared from wild type (wt) or *PAR2<sup>-/-</sup>* mice and exposed to sub-maximally (0.1 nM) or supra-maximally (1 nM) stimulating concentrations of caerulein (caer). Acini from both groups showed only oscillatory responses to 0.1 nM caerulein and only peak-plateau responses to 1 nM caerulein. **SUPPLEMENTAL FIGURE 4. Neither TFLLR nor LRGILS alter the frequency of calcium transient patterns observed in wild type acini exposed to Na-taurocholate and SBTI.** Small pancreatic acini were freshly prepared from wild type mice and exposed to increasing concentrations of Na-taurocholate (NaT) or pre-incubated with 5 μM soybean trypsin inhibitor (SBTI) for 30 min prior to addition of Na-taurocholate. For selected acini, either 1 mM SLIGRL, TFLLR or LRGILS were added at the time of Na-taurocholate addition. Panel *A* shows representative calcium transients from single acinar cells under the conditions described. The three types of response can been seen (marked in each box). Type I consists of oscillations only. Type II consists of oscillations superimposed on a peak plateau. Type III consists of small peak and a sudden and persistent decline of the baseline indicating cell lysis. Panel *B* shows quantitation of the response patterns observed in single acinar cells pre-treated with SBTI and then exposed to either Na-taurocholate alone or to Na-taurocholate along with either TFLLR or LRGILS. Black areas indicate type III response, hatched areas indicate type II response and white areas indicate type I response. Note that neither TFLLR nor LRGILS can reverse the SBTI effect on calcium response-type frequency.

SUPPLEMENTARY FIGURE 5. Neither TFLLR nor LRGILS alter LDH leakage induced in wild type acini by Na-taurocholate or caerulein. Small pancreatic acini were freshly prepared from wild type mice. They were incubated for 30 min in the presence of buffer alone, buffer containing Na-taurocholate (NaT) (0.3%), or buffer containing caerulein (Caer) (100 nM). Selected acini were preincubated for 30 min with 5  $\mu$ M SBTI alone (closed columns), SBTI followed by 1 mM TFLLR and Na-taurocholate or caerulein (hatched columns) or SBTI followed by LRGILS and Na-taurocholate or caerulein (gray columns). Results reflect mean values obtained from 3 independent experiments and vertical bars denote +/- SEM. Asterisks denote p<0.05 and NS denotes non-significance of differences when bracketed groups were compared. Note that neither TFLLR nor LRGILS could reverse the SBTI effect on LDH release.









