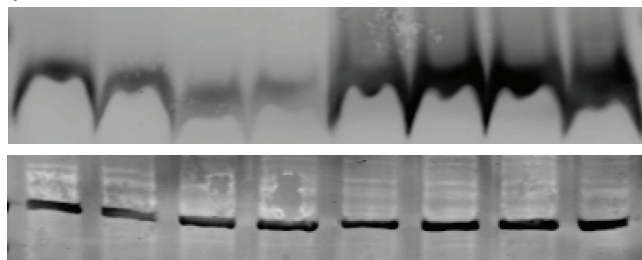
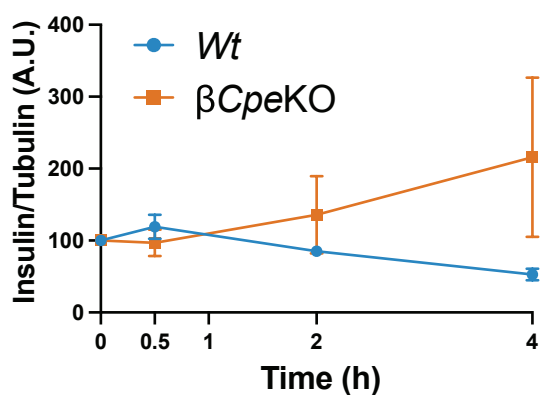


**A***Wt* $\beta$ CpeKO

Chx (h) 0 0.5 2 4 0 0.5 2 4

Insulin

Tubulin

**B****Insulin****C** $\beta$ CpeKO

Mouse #1

Mouse #2

Mouse #3

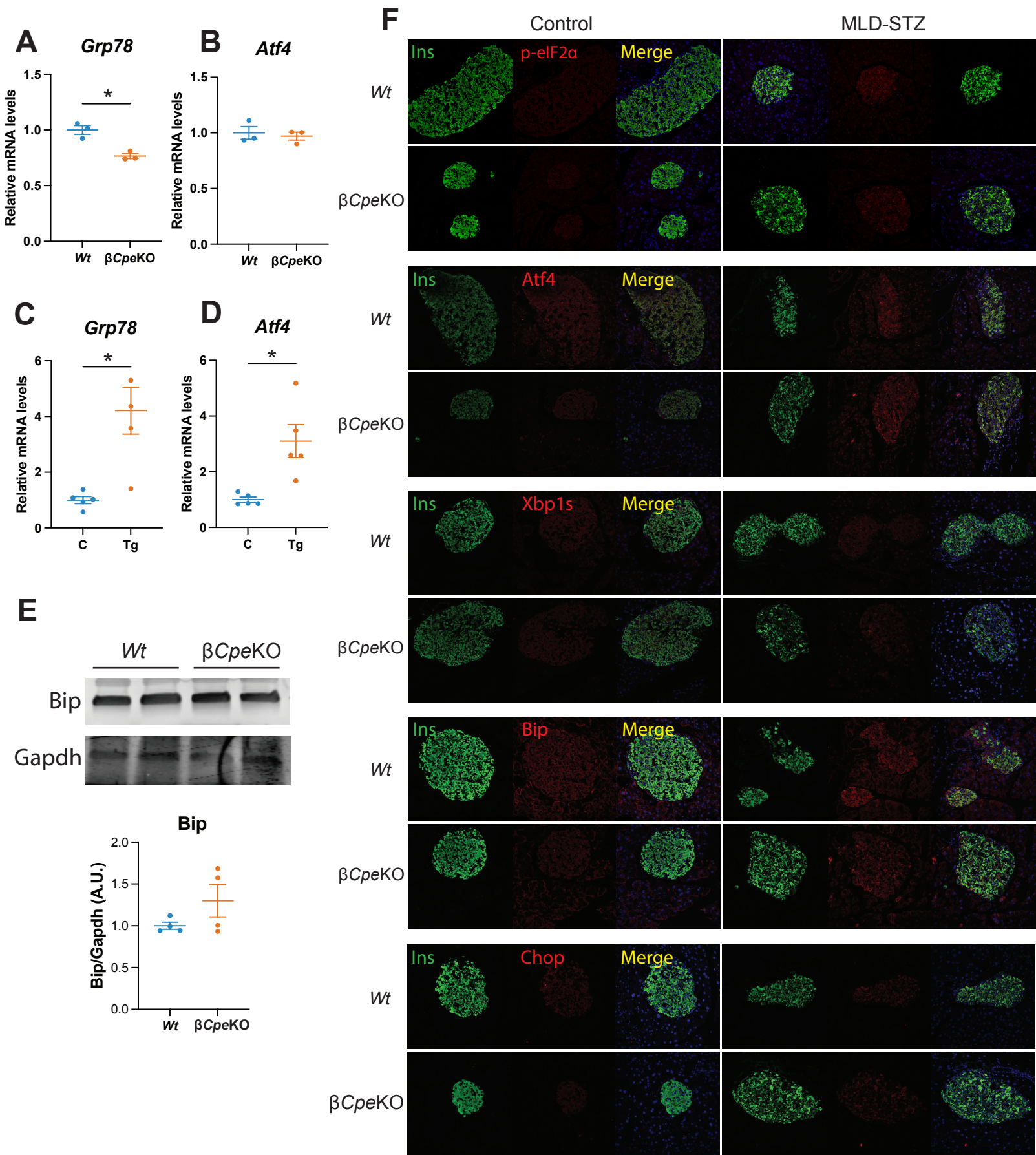
Chx (h) 0 0.5 2 4 0 0.5 2 4 0 0.5 2 4

Insulin

Tubulin

**Supplemental Figure 1**

Islets from *Wt* and  $\beta$ CpeKO mice were treated with 100  $\mu$ g/mL cycloheximide (Chx) for 0, 0.5, 2, or 4 hours, and islet lysates were analyzed by SDS-PAGE and immunoblotting using anti-insulin and anti-tubulin antibodies. **(A)** Representative immunoblot images **(B)** Quantitative analysis (n=3) **(C)** Samples from the  $\beta$ CpeKO group were re-analyzed by immunoblotting with less protein loaded in each wells to evaluate insulin protein levels. Data are expressed as mean $\pm$ SEM, n=3.



### Supplemental Figure 2

(A, B) qRT-PCR analysis of *Grp78* and *Atf4* levels in freshly isolated islets from *Wt* and  $\beta$ CpeKO mice, with (C, D) ER stress inducer Thapsigargin (Tg, 1mM for 4 hours)- treated *Wt* mouse islets as positive control. (E) Islets Bip protein levels were analyzed by immunoblotting using antibody specific for Bip and Gapdh (F) Representative islet images of non-treated or MLDSTZ-treated *Wt* and  $\beta$ CpeKO mice. Paraformaldehyde-fixed paraffin-embedded mouse pancreatic sections were immunostained with antibodies specific for insulin (Ins), phospho-eIF2 $\alpha$  (p-eIF2 $\alpha$ ), Atf4, spliced Xbp1(Xbp1s), Bip, and Chop. Data were expressed as mean $\pm$ SEM. \* $p$ <0.05