**Supplemental Data**

**Supplemental Table 1.** Body weight as well as blood glucose and plasma insulin concentrations in the fed state for WT, Ins-*Cre*, and C/EBPβ$^{flox/flox}$ mice at 8 weeks of age. Data are means ± SEM from four mice of each genotype.

**Supplemental Figure 1.** (**A**) Gene targeting strategy for C/EBPβ. Black triangles and shaded rectangles indicate loxP sites and the C/EBPβ-coding exon, respectively. See Methods for details. (**B**) Southern blot analysis of ES cell clones. Genomic DNA from WT ES cells (lane 1), an ES cell clone with a targeted allele (lane 2), or an ES cell clone with a floxed allele (lane 3) was digested with XbaI and subjected to Southern blot hybridization with the external probe shown in (**A**). The expected sizes of the hybridizing fragments are also indicated in (**A**).

**Supplemental Figure 2.** Blood glucose concentrations during insulin tolerance tests are shown for control (C/EBPβ $^{flox/flox}$; open circles; n=5) and βC/EBPβ$^{-/-}$ (black circles; n=6) mice.

**Supplemental Figure 3.** Blood glucose and plasma insulin concentrations of WT, Ins-*Cre*, Akita(Ins2$^{WT/C96Y}$), and Akita(Ins2$^{WT/C96Y}$) × Ins-*Cre* mice in the fed state and at the indicated ages. Data are means ± SEM from at least six mice of each genotype.

**Supplemental Figure 4.** Southern blot analysis of C/EBPβ transgene in the islets of WT, Akita(Ins$^{WT/C96Y}$), TG1, and TG2 mice.

**Supplemental Figure 5.** Quantification of the expression or phosphorylation levels of the proteins analyzed in Figure 5A. Data are means ± SEM from four independent experiments. *$P < 0.05$, **$P < 0.01$.

**Supplemental Figure 6.** Quantification of the expression or phosphorylation levels of the proteins analyzed in Figure 6G. Data are as means ± SEM from four independent experiments. *$P < 0.05$.

**Supplemental Figure 7.** INS-1 cells were transfected with the *GRP78* promoter-luciferase gene construct, a vector for full-length ATF6α or a vector for C/EBPα or β, or the corresponding empty vector (Mock). The cells were subsequently harvested and assayed for luciferase activity.

**Supplemental Figure 8.** ChIP assay of the *Grp78* promoter in islets isolated from TG2. Lysates were subjected to immunoprecipitation (IP) with antibodies to ATF6 or with control IgG, and DNA in the resulting precipitates was subjected to PCR with primers specific for the *Grp78* promoter.

**Supplemental Figure 9.** ChIP assay of the *Grp78* promoter in INS1 cells infected with a retrovirus encoding either C/EBPβ or the corresponding empty vector (Mock). Cell lysates were subjected to immunoprecipitation (IP) with antibodies to C/EBPβ or with control normal mouse globulin, and DNA in the resulting precipitates was subjected to PCR with primers specific for the *Grp78* promoter.

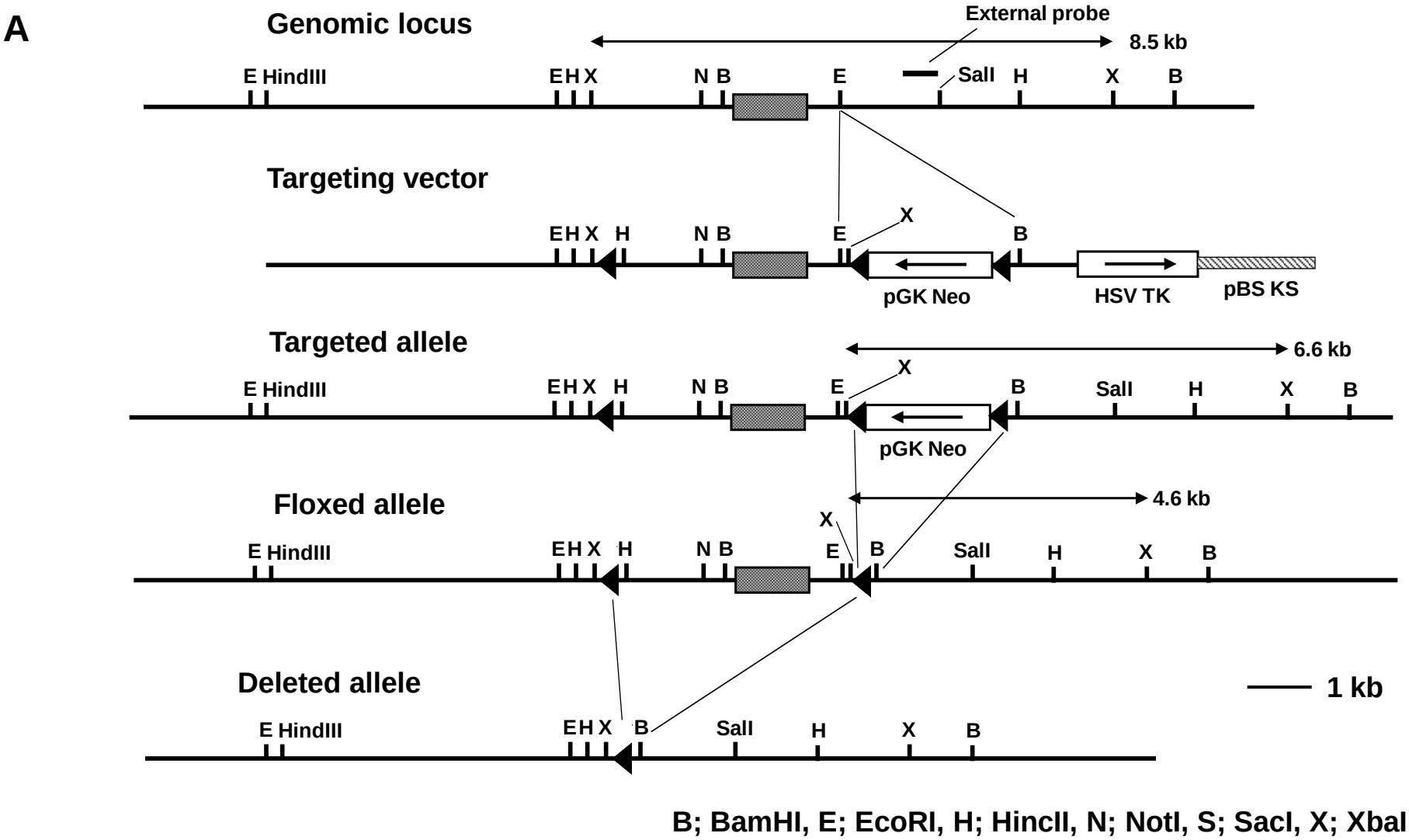
**Supplemental Figure 10.** INS1 cells were transfected with the *GRP78* promoter–luciferase gene construct, a vector for full-length ATF6α or the corresponding empty vector, and a vector for C/EBPβ or mutated C/EBPβ ($C_{296}S$) or the corresponding empty vector (Mock). The cells were subsequently harvested and assayed for luciferase activity. Data are means ± SEM from 3 independent experiments. $^{**}P < 0.01$.

**Supplemental Figure 11.** HepG2 cell lysates were subjected to immunoprecipitation with antibodies to C/EBPβ or with normal rabbit serum, and the resulting precipitates were subjected to immunoblot analysis with antibodies to ATF6α and to C/EBPβ. Portions of the original cell lysates corresponding to 5% of the input for immunoprecipitation were similarly analyzed.

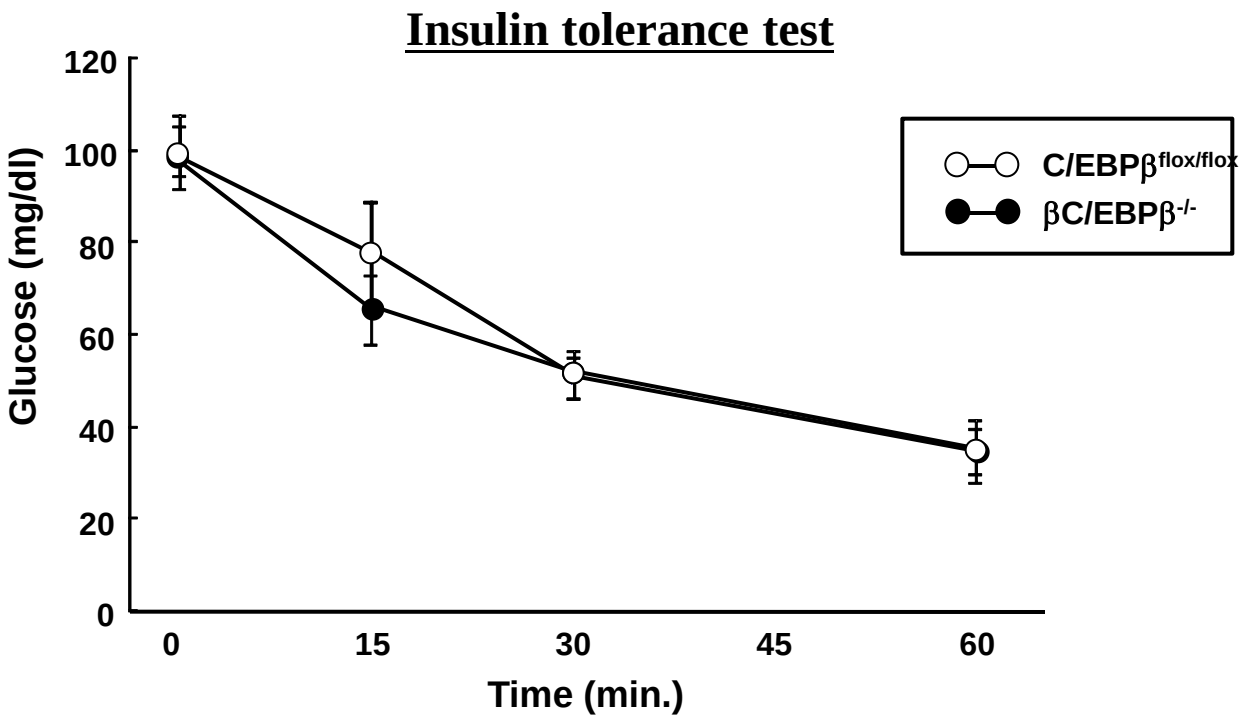
Matsuda et al Supplement Table 1

| | Mice | | |
|---|---|---|---|
| Parameter | WT | Ins-*Cre* | C/EBPβ$^{flox/flox}$ |
| Body weight (g) | 23.5 ± 1.3 | 23.2 ± 1.1 | 22.0 ± 0.5 |
| Blood glucose (mg/dl) | 129.8 ± 6.3 | 132.0 ± 6.5 | 144.2 ± 5.2 |
| Plasma insulin (ng/ml) | 0.53 ± 0.19 | 0.52 ± 0.08 | 0.54 ± 0.06 |

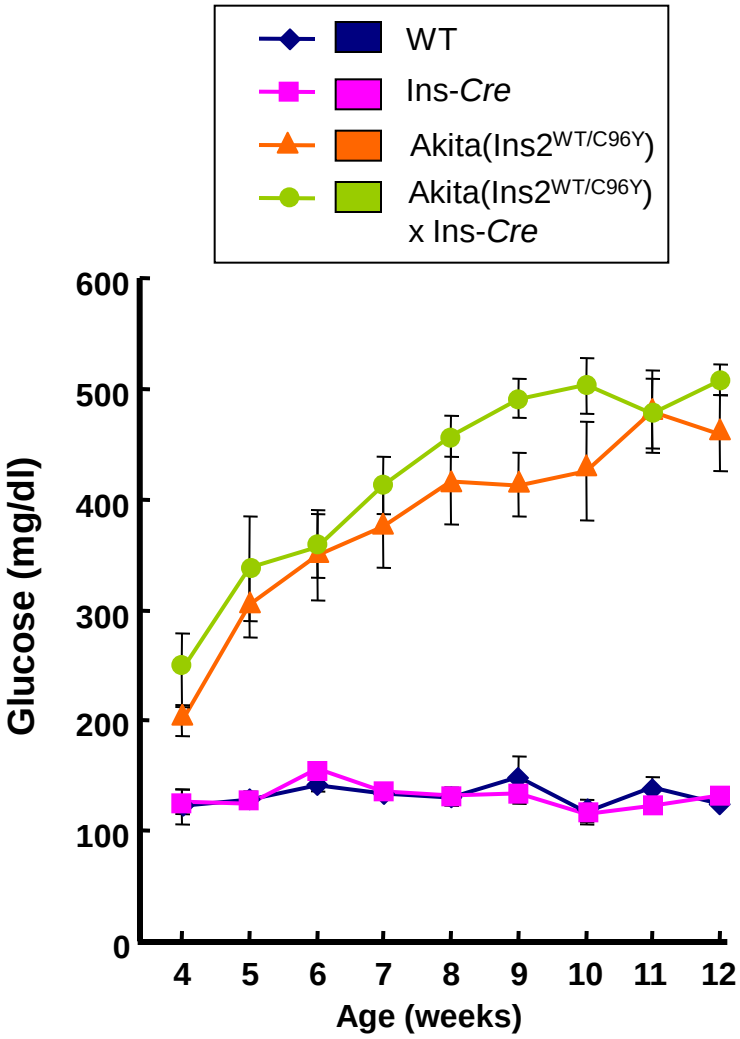
Body weight as well as blood glucose and plasma insulin concentrations in the fed state for wild-type, Ins-*Cre*, and C/EBPβ$^{flox/flox}$ mice at 8 weeks of age. Data are means ± SEM from four mice of each genotype.

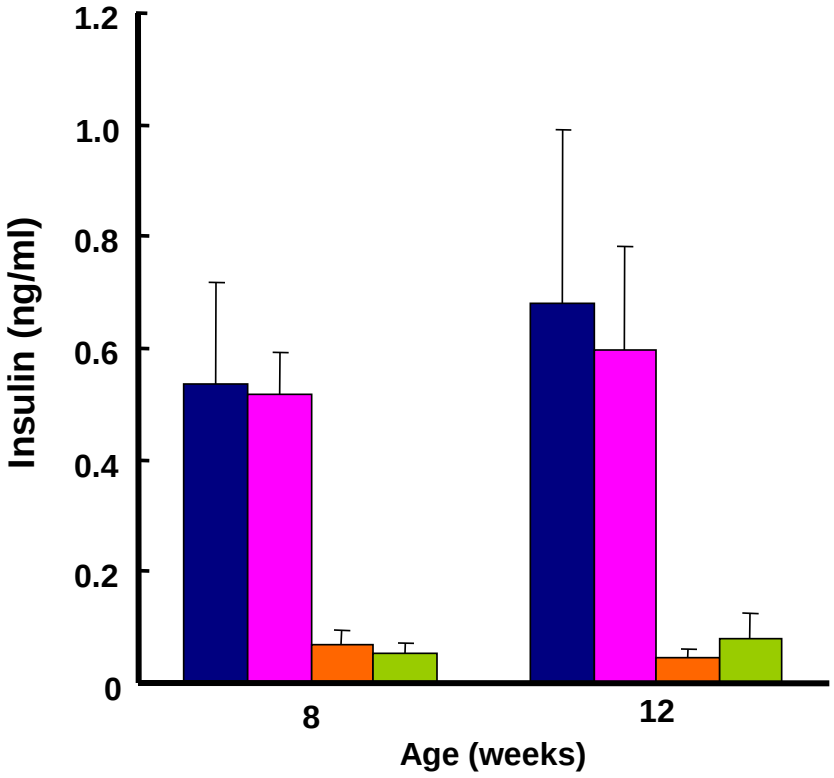



Matsuda et al Supplementary Figure 1

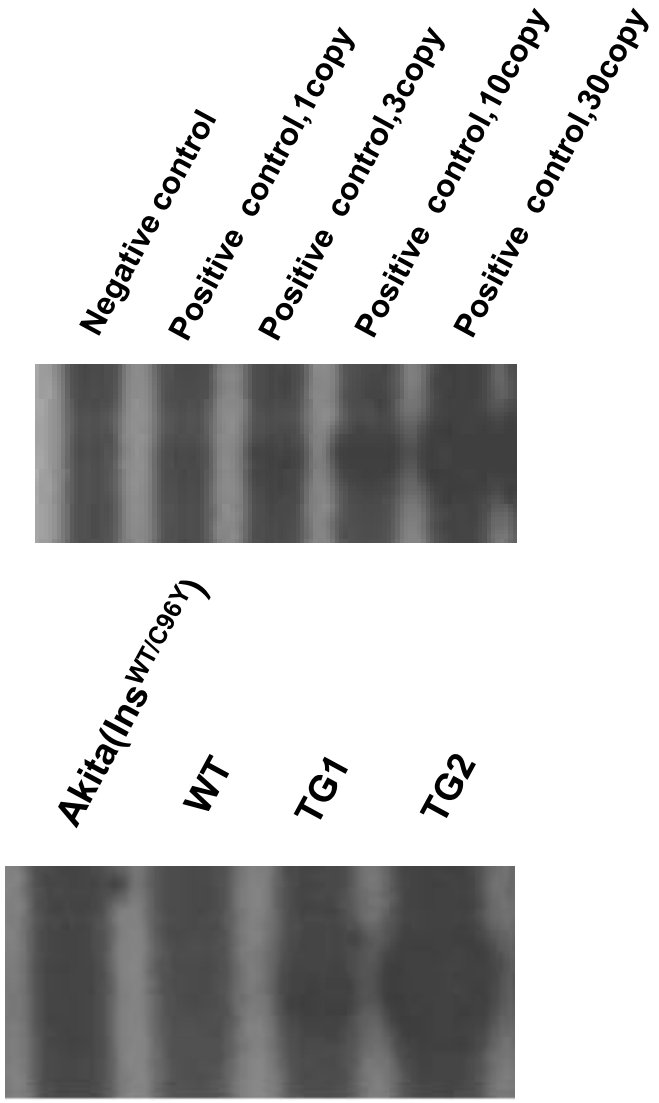


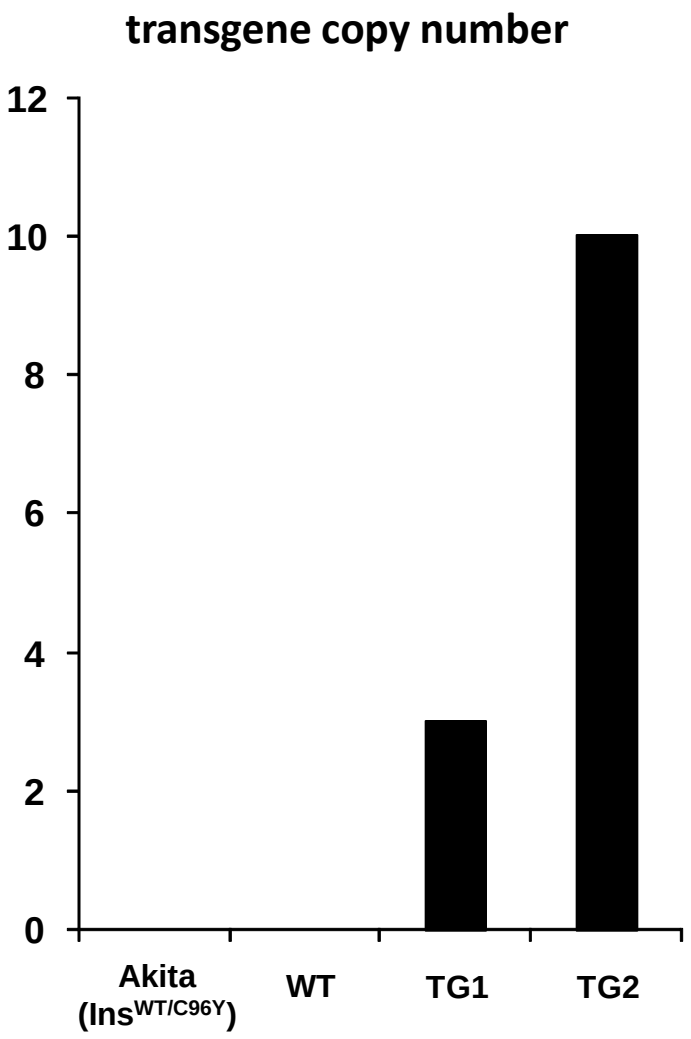

Matsuda et al Supplementary Figure 2



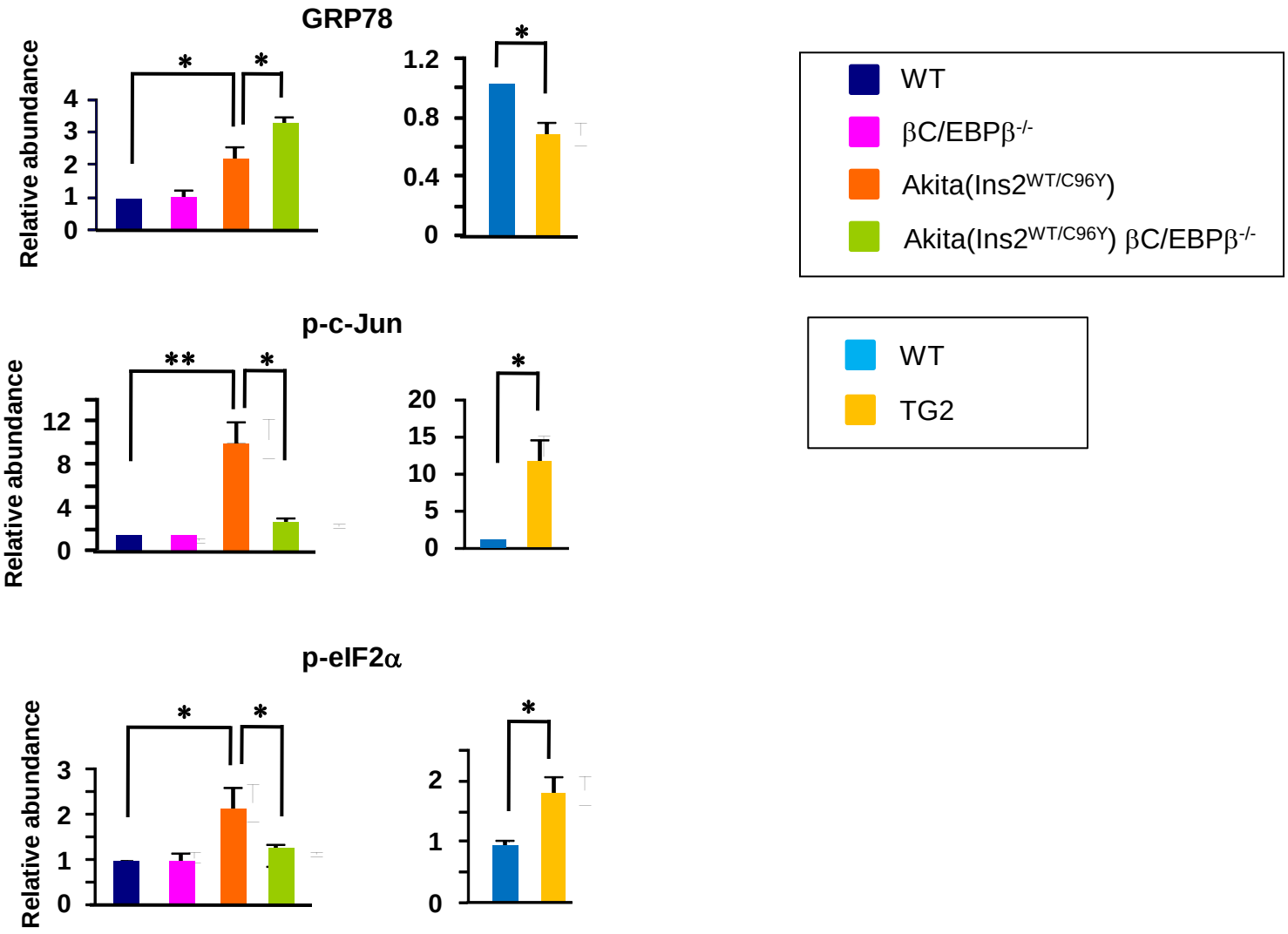




**Matsuda et al Supplementary Figure 3**

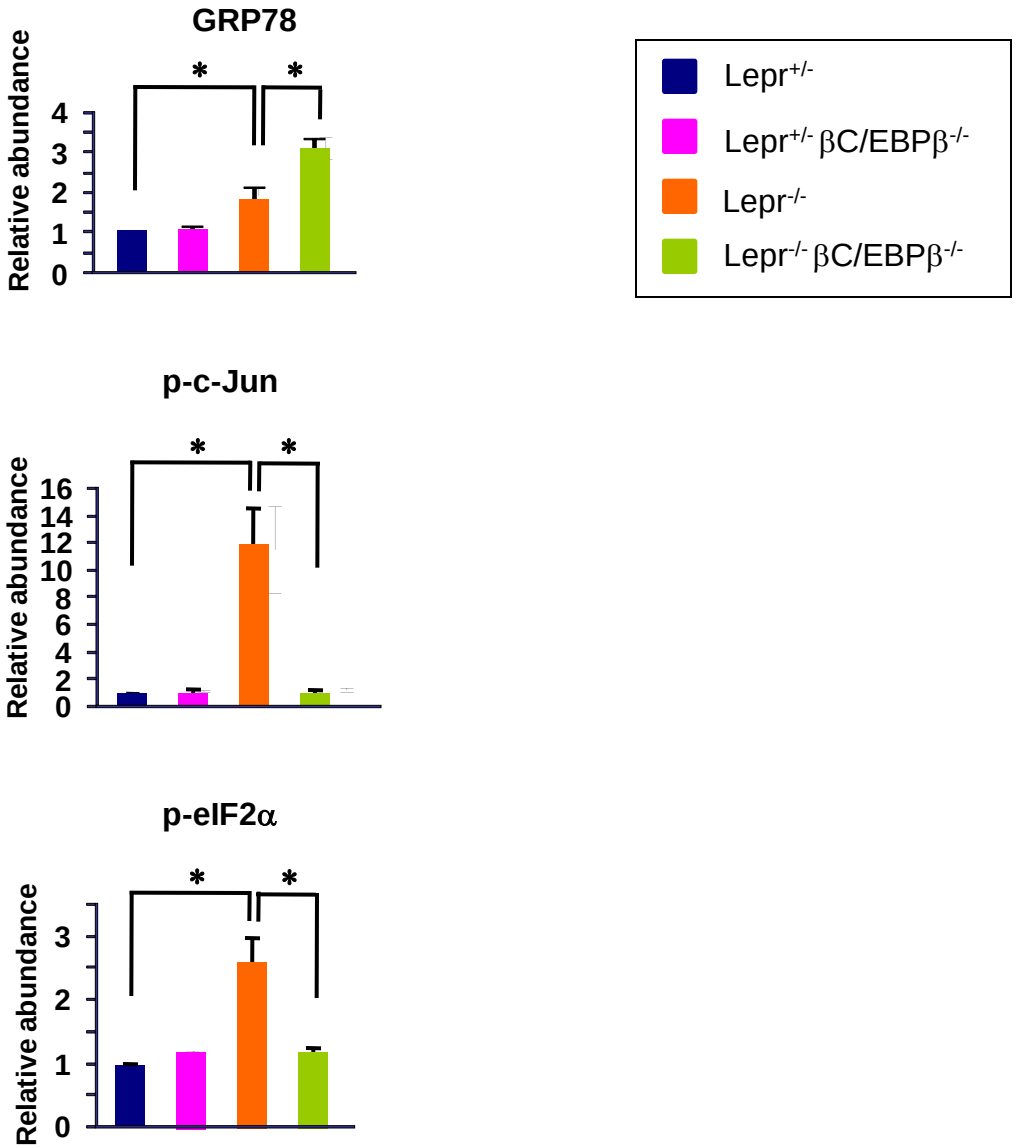


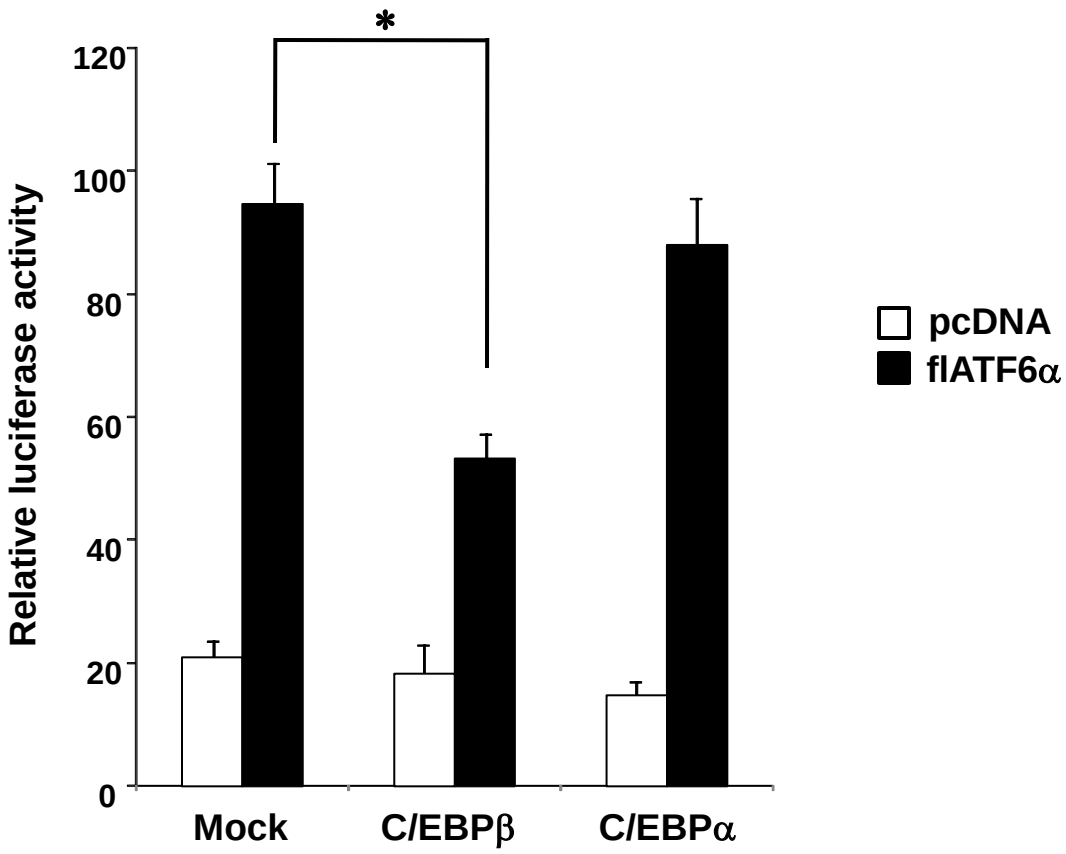

**Matsuda et al Supplementary Figure 4**



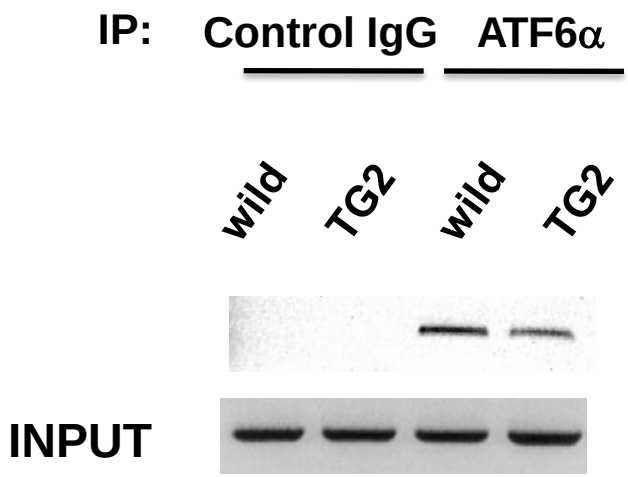

**Matsuda et al Supplementary Figure 5**



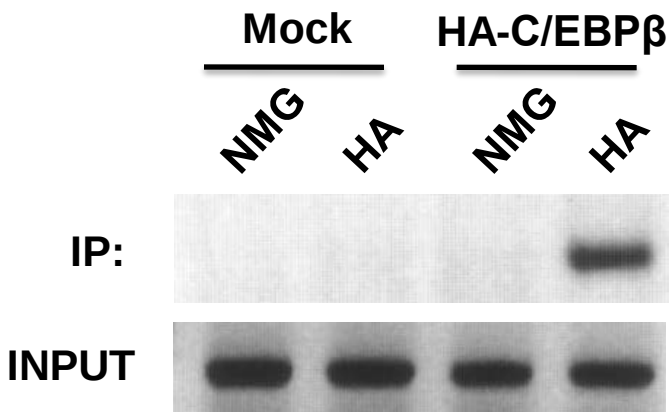

**Matsuda et al Supplementary Figure 6**



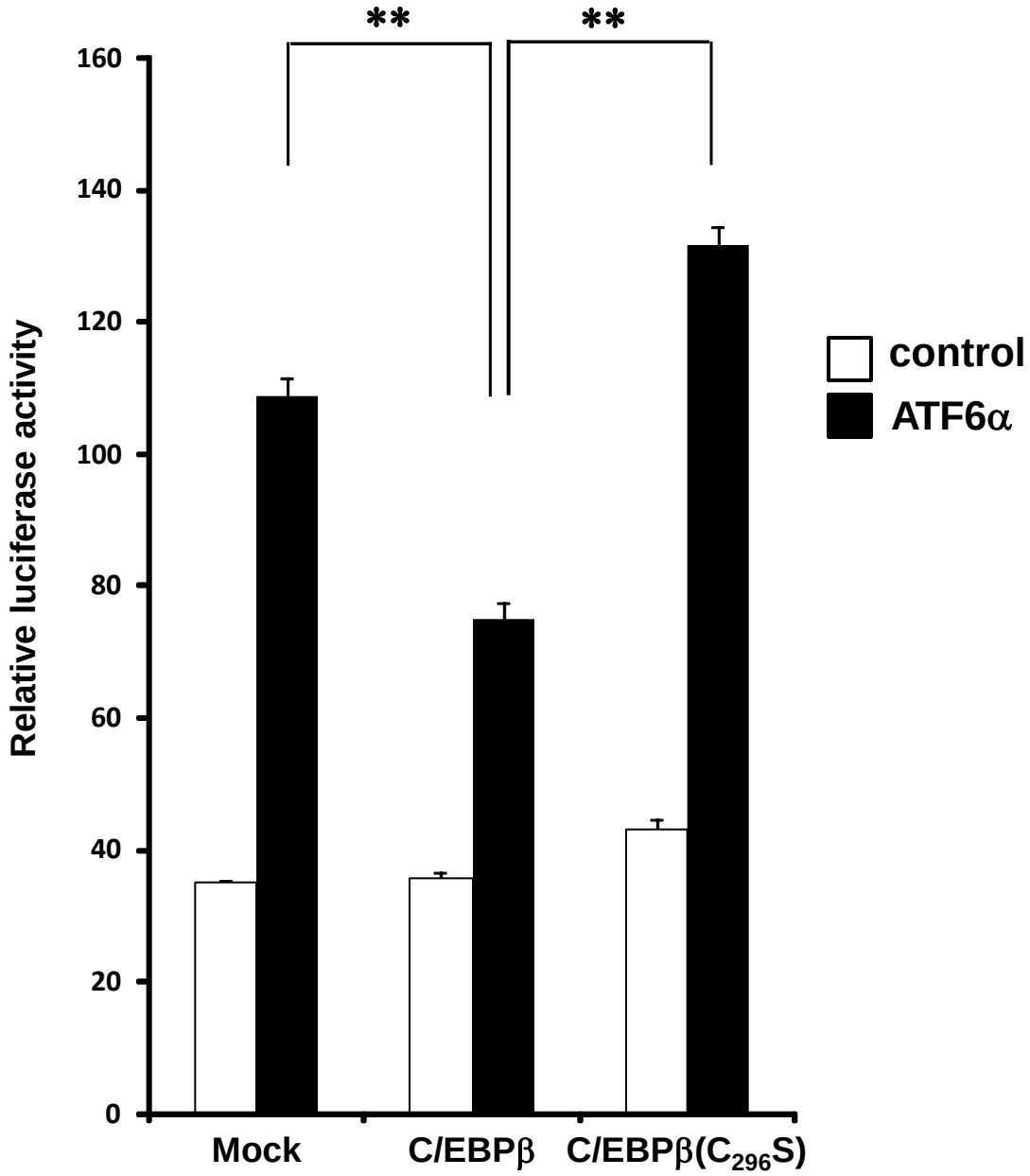

Matsuda et al Supplementary Figure 7



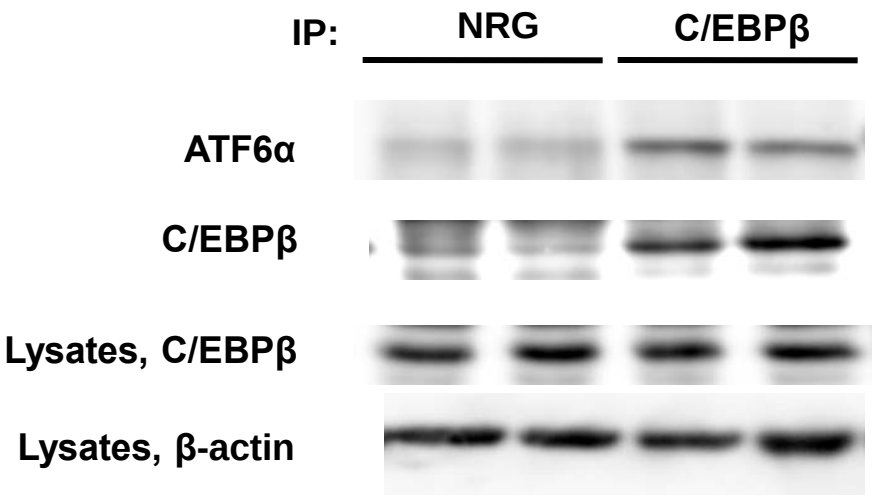

Matsuda et al Supplementary Figure 8




Matsuda et al Supplementary Figure 9




Matsuda et al Supplementary Figure 10




Matsuda et al Supplementary Figure 11