



**Supplementary Figure 1. Tpl2 inhibitor specifically blocks Tpl2 activity effects and Tpl2<sup>-/-</sup> have no improvement of survival nor function.** **a-b:** Caspase-3/7 activity in mouse islets from **a:** WT (Tpl2<sup>+/+</sup>) or **b:** Tpl2-deficient (Tpl2<sup>-/-</sup>) untreated (Ctr) or treated for 24 h with cytokine mix (CK) with or without Tpl2-I (3  $\mu$ M). Data are mean  $\pm$  SEM (N=8/group). \*P<0.05 vs CK (one-way ANOVA). **c-d:** Insulin secretion in response to glucose (3mmol/L (G3) vs 15mmol/L (G15)) on the same conditions that **a** and **b**. Data are mean  $\pm$  SEM (N=8/group). \*P<0.05 G15 vs G3 (one-way ANOVA). **e and f:** intraperitoneal (*ip*) Glucose tolerance test performed in Tpl2<sup>+/+</sup> and Tpl2<sup>-/-</sup> mice (**e**), with associated plasma insulin level (**f**).