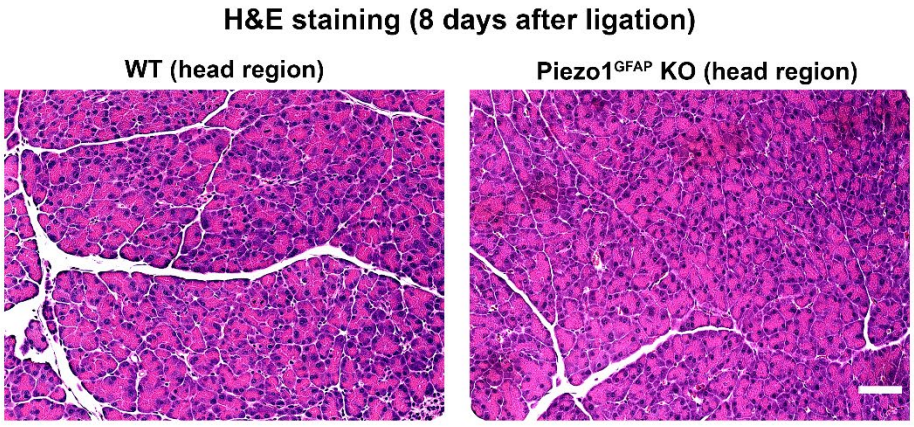
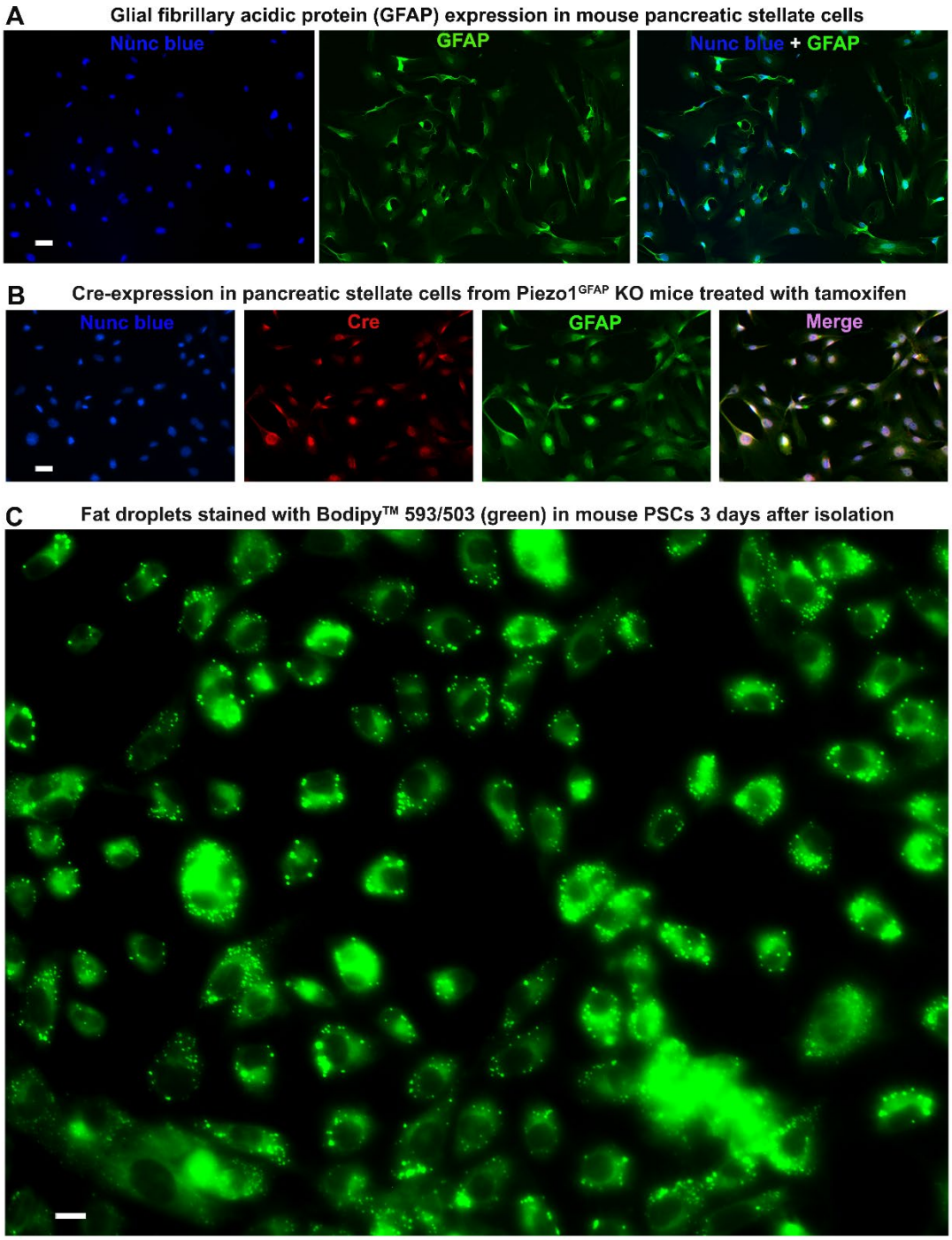
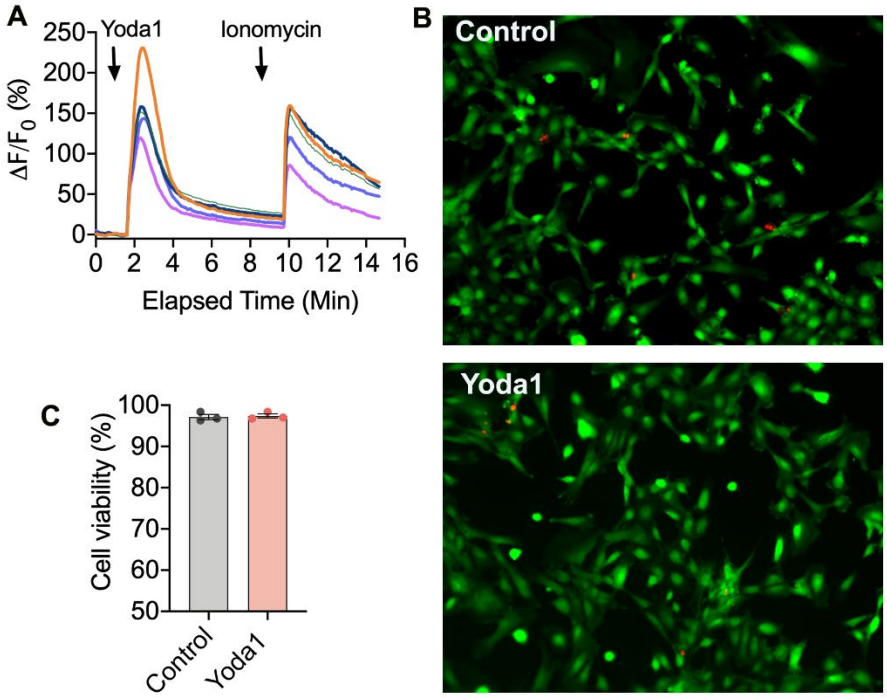
## Supplemental Materials



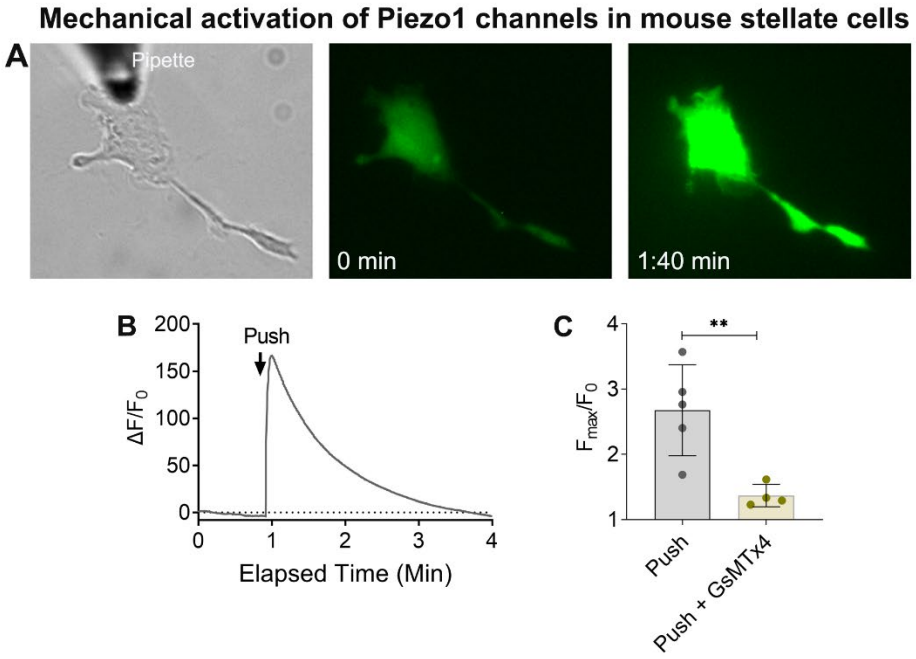

**Supplemental Figure 1. Pancreatic duct ligation at tail region did not affect the head of the pancreas.** Representative H&E stained images of the pancreatic head region of wildtype (WT) and Piezo1$^{GFAP}$ KO mice 8 days after PDL (n = 3-7).



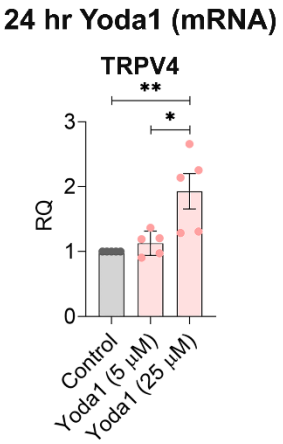

**Supplemental Figure 2. Piezo1 deletion in GFAP-expressing PSCs. (**A) Images showing expression of GFAP (green) in mouse PSCs after 3 days in culture. Cell nuclei were stained with Nunc blue. (B) PSCs expressing Cre protein from the mouse line B6.Cg-Tg (GFAP-cre/ERT2); *Piezo1*$^{fl/fl}$ after tamoxifen injection (referred to as Piezo1$^{GFAP}$ KO mice) confirm deletion of Piezo1 in PSCs. Scale bar: 20 µm. All cells (Nunc blue), expressing Cre protein, and GFAP appear as merged images. (C) Quiescent PSCs containing perinuclear fat droplets (stained with Bodipy™ 593/503) were cultured on a Matrigel coated plate. Scale bar: 10 µm.




**Supplemental Figure 3. High dose Yoda1 did not affect PSC viability and membrane integrity.** (A) Mouse PSCs responded to ionomycin (1 µM) after Yoda1 (25 µM) treatment. (B and C) PSCs were treated with Yoda1(25 µM) for 2 hrs afterwhich the viability of stellate cells was analyzed using the Live/Dead Cell Imaging Kit (Thermo Fisher Scientific, Catalog # R37601). Representative images show live (green) and dead (red) cells. (C) The graph represents viable cells with and without Yoda1 treatment (n=3 experiments).




**Supplemental Figure 4. Mechanical pushing increases $[Ca^{2+}]_i$ in PSCs.** (A) Bright field and live-cell images of mouse PSC at time 0 and at 1:40 (min:s) after mechanical pushing with a blunt tip glass pipette for 1 sec. (B) Representative $[Ca^{2+}]_i$ profile from a single mouse PSC during the course of mechanical pushing. (C) Graph showing peak $[Ca^{2+}]_i$ levels following mechanical pushing in PSCs with and without GsMTx4 (2.5 μM). **P<0.01, n=4-5.




**Supplemental Figure 5. Piezo1 agonist, Yoda1, upregulates TRPV4 expression in PSCs.** mRNA levels of TRPV4 in human PSCs 24 hrs after treatment with Yoda1 (5 μm and 25 μM). *P<0.05, **P<0.01, n=5.