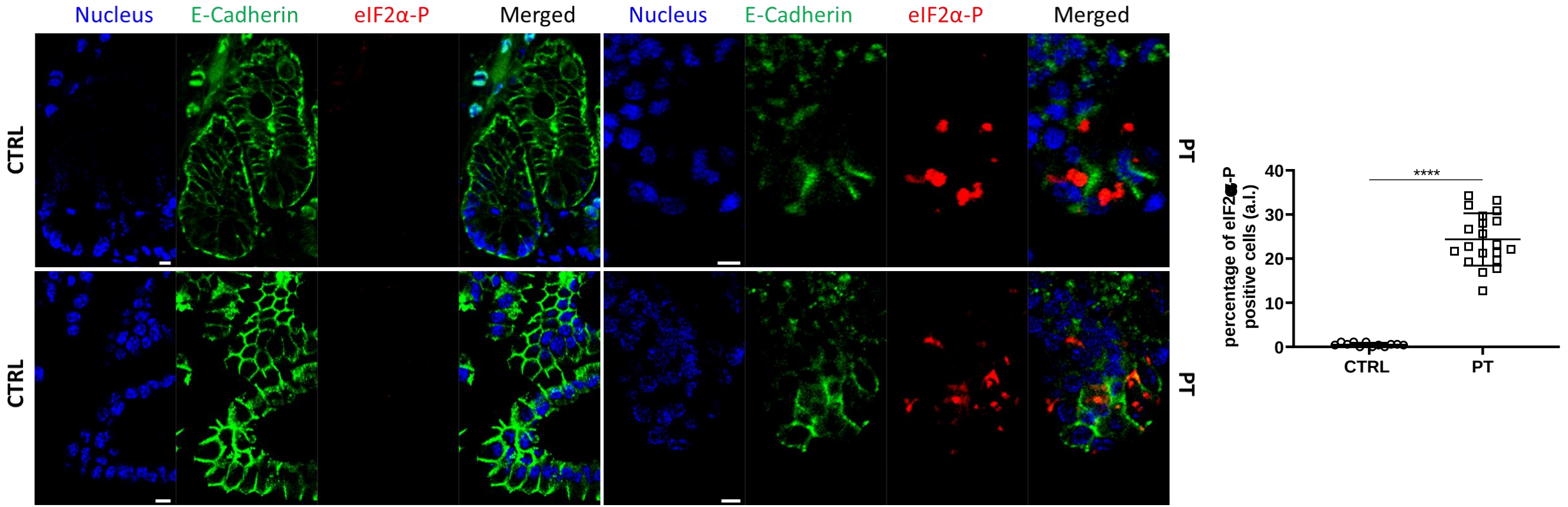
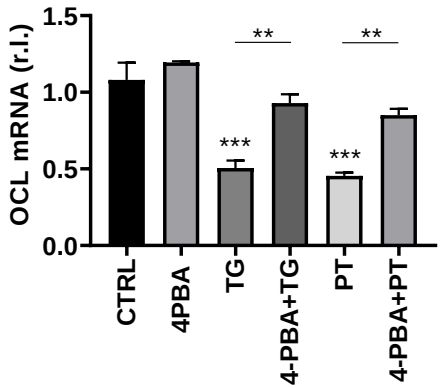
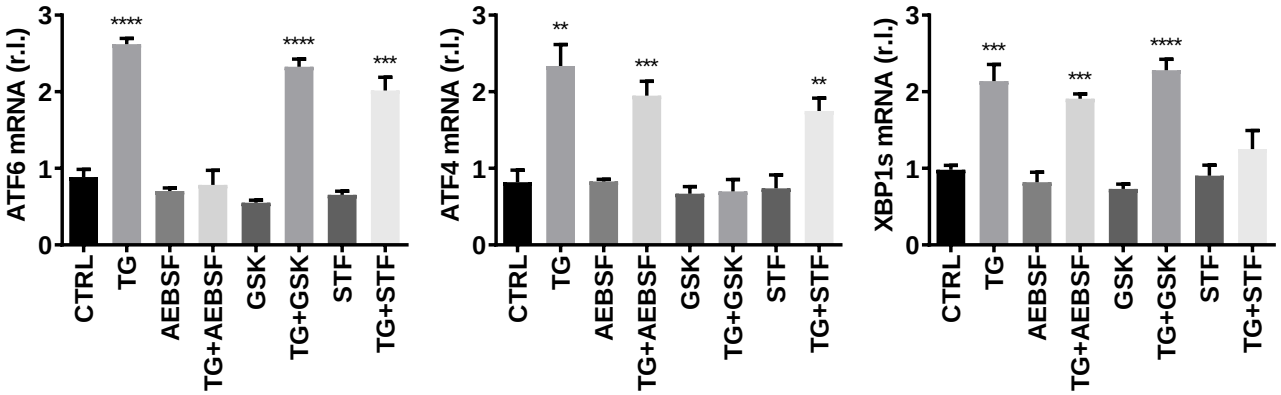


Supplementary S1. UPR induction in IECs, by PT exposure. The small intestine from GF mice were cultivated in the GEVS and unexposed (CTRL) or exposed to PT (2.5 mg/mL) for 9h, and the ER stress marker eIF2α-P was evaluated (red) in IEC evidenced by anti-E-Cadherin (green), while nuclei were stained by DAPI (blue; left). Representative images of experiment performed in triplicate; scale bar = 10 µm. The percentage of eIF2α-P positive cells among total IECs was also calculated and reported as mean ± s.d. (right panel); **** = $p < 0.0001$.



Supplementary S2. UPR regulates the expression of Occludin in IECs. The small intestine from GF mice were cultivated in the GEVS and unexposed (CTRL) or exposed to 4PBA (3 ⍰M), PT (2.5 mg/mL), or TG (5 ug/mL) alone or in combination for 16h, and the expression of occludin (OCL) was evaluated by qPCR. Data are representative of three independent experiments performed in triplicate. Histograms represent mean±s.d.; **p < 0.01; ***p < 0.001.



Supplementary S3. Specific inhibition of the three ER stress branches. Caco-2 cells were stimulated 9h with PT (1 mg/ml) alone or in the presence of AEBSF (500 μM; ATF6 activation inhibitor), GSK2606414 (GSK, 5 μM; PERK inhibitor), or STF-083010 (STF, 60 μM; IRE1α inhibitor) and the expression of ATF6 (left panel), ATF4 (middle panel), or sliced XBP1 (XBP1s, right panel) was evaluated by qPCR.

Data are representative of three independent experiments performed in triplicate. Histograms represent mean±s.d.; **p < 0.01; ***p < 0.001; ****p < 0.0001.